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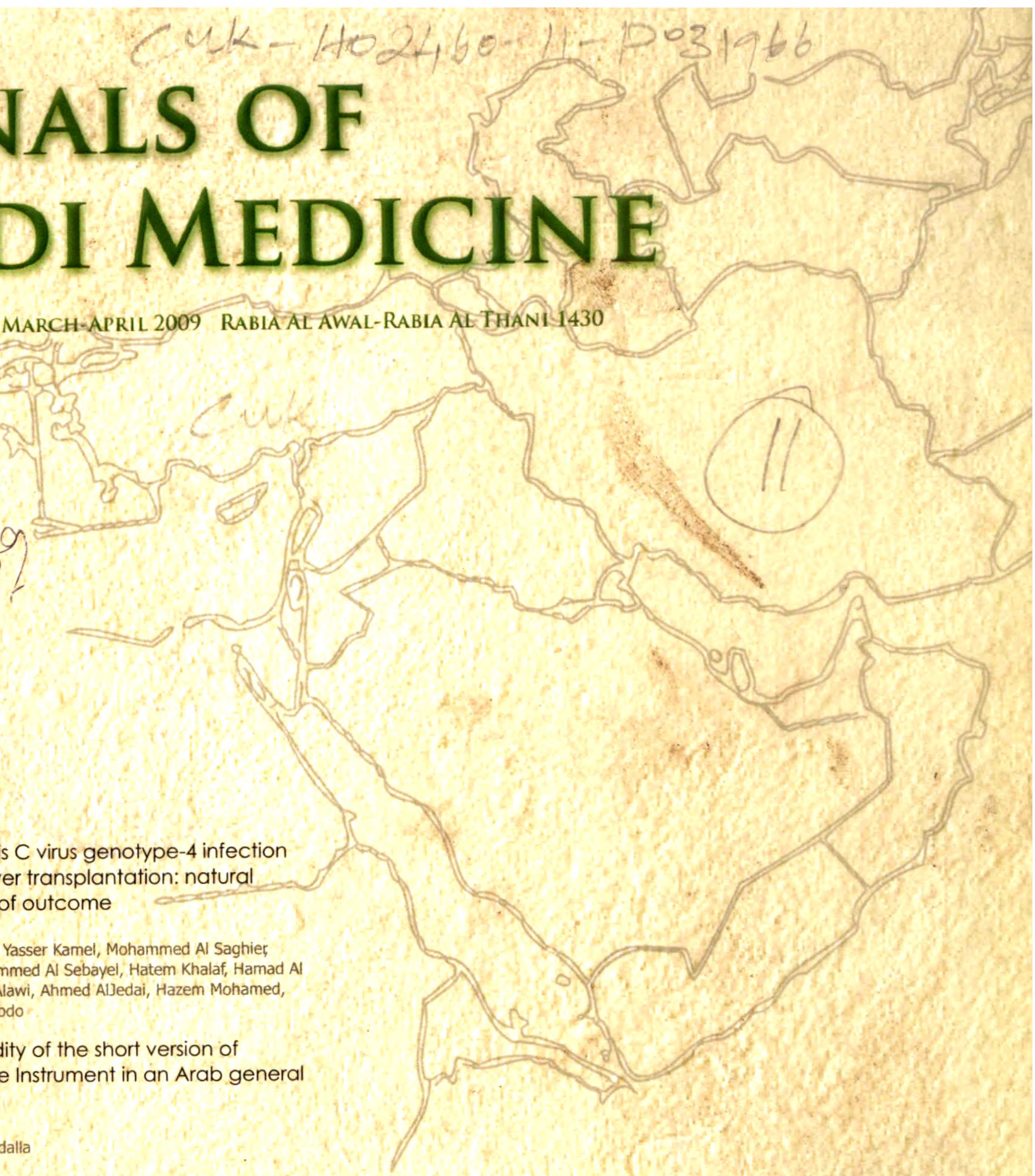

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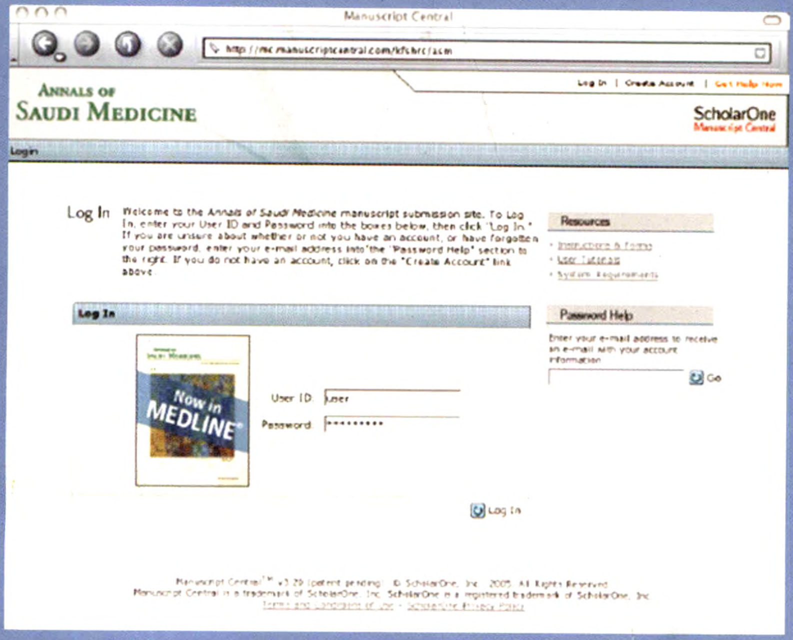
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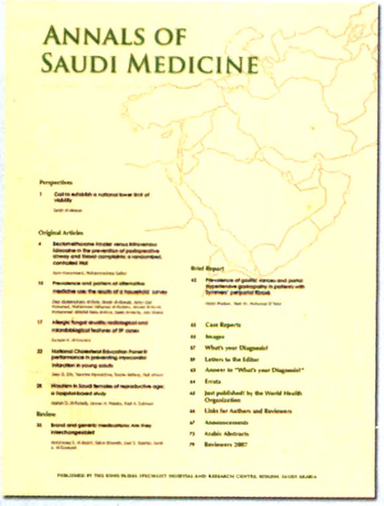

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The *Annals of Saudi Medicine* is published bimonthly by King Faisal Specialist Hospital & Research Centre. Arabic abstracts are prepared, in association with Dr. M. Zuheir Al-Kawi, by the staff of the Office Services Department of King Faisal Specialist Hospital & Research Centre.

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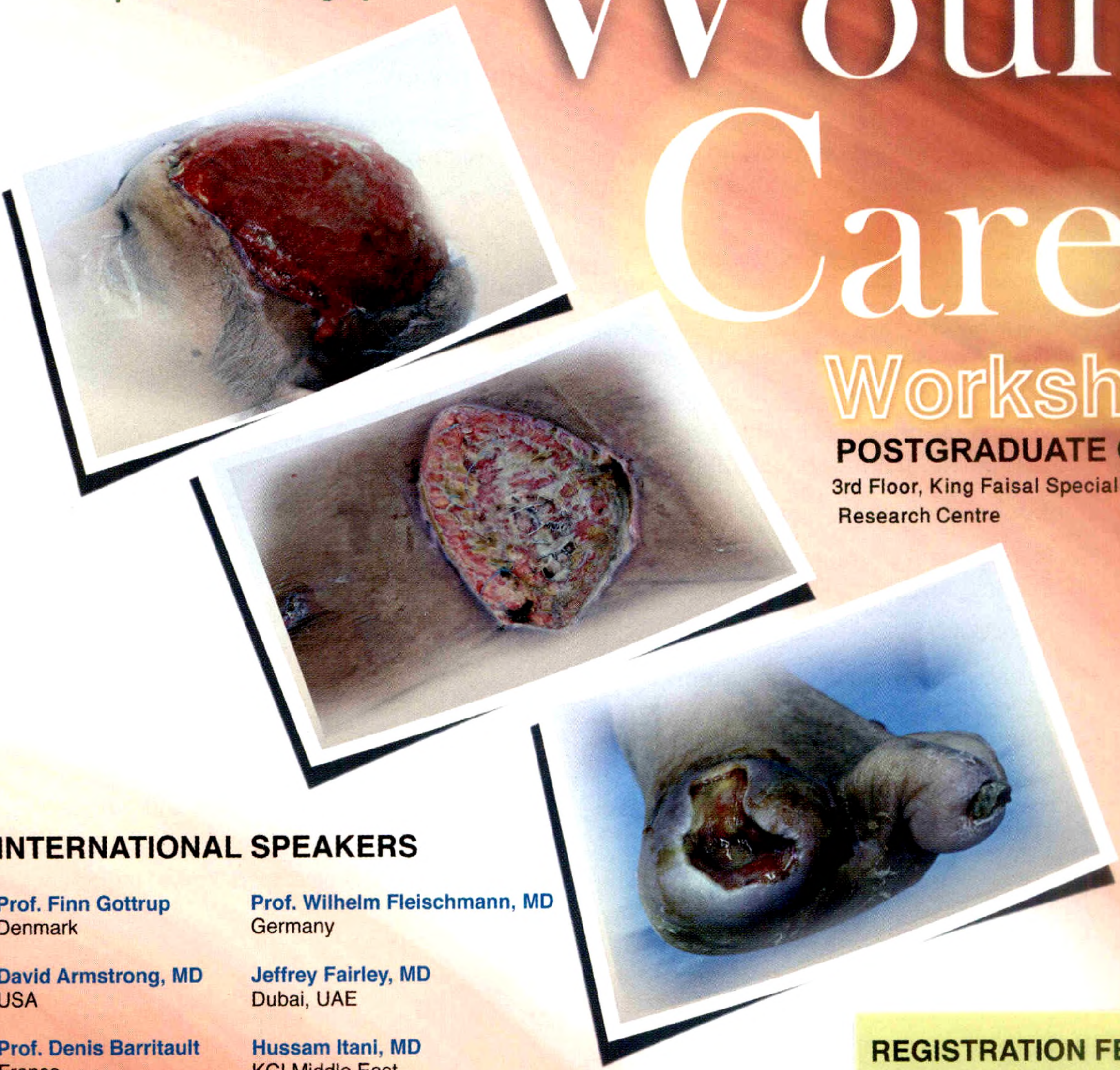

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SUMMARIES

LIVER TRANSPLANTATION

Recurrence of hepatitis C virus genotype-4 infection following orthoptic liver transplantation: natural history and predictors of outcome

Mudawi and colleagues analyzed data on all patients (n=116) who underwent orthoptic liver transplantation for liver disease related to hepatitis C virus (HCV) infection who were followed at KFSHRC from 1991 to 2006 and had recurrent HCV infection (n=46, 39.7%). Twenty-nine patients (63%) were infected with HCV genotype 4. In a multivariate logistic regression model, only viral load at the time of biopsy was a predictor of higher fibrosis stage in patients with recurrent HCV infection. There were no significant differences between HCV genotype 4 and other genotype patients in rejection or survival rates during the mean 38.5 months of follow-up. The authors concluded that HCV recurrence following orthoptic liver transplantation in genotype 4 patients is not different from patients with other genotypes.

PSYCHIATRY

The reliability and validity of the short version of the WHO Quality of Life Instrument in an Arab general population

Because of rising interest in quality-of-life (QOL) research in Arabian countries, Ohaeri and Awadalla assessed the reliability and validity of an Arabic translation of the WHOQOL-BREF in a nationwide sample of Kuwaiti subjects. The authors report data for 3303 participants, who were representative of the six governates. They concluded that the Arabic translation of the instrument had impressive reliability and validity indices. Their data support the impression that the WHOQOL-BREF is a cross-culturally valid generic instrument that addresses health-related QOL, contextual issues, and subjective well-being.

CARDIOVASCULAR SURGERY

Management of traumatic brachial artery injuries: A report on 49 patients

Ekim and Tuncer describe their experience with 49 patients who underwent surgical repair procedures for brachial artery injuries over an 8-year period. The mechanism of injury was penetrating in 45 cases, including 24 stab injuries. Treatment included primary arterial repair in 5 cases, end-to-end anastomosis in 28 cases, interposition vein graft in 15 cases, and interposition-ringed polytetrafluoroethylene graft in 1 case. Associated injuries were common. Fifteen patients developed postoperative complications, but only one underwent amputation. The authors conclude that prompt and appropriate management of brachial artery injuries, attention to associated injuries, and a readiness to revise the vascular repair early in the event of failure will maximize patient survival and upper extremity salvage.

CARDIOTHORACIC SURGERY

Extracorporeal circulatory systems in the interhospital transfer of critically ill patients: experience of a single institution

Haneya and colleagues report on 38 interhospital transfers involving extracorporeal support over a 7-year period, including 29 patients with respiratory failure and 9 with predominately cardiac failure. The respiratory failure patients were provided with pumpless extracorporeal lung assist (PECLA) or veno-venous extracorporeal membrane oxygenation (ECMO), while the cardiac failure patients underwent implantation of extracorporeal life support (ECLS). Transportation was uneventful in all cases with no technical failures. About two-third of patients were weaned from the systems within a few days and about half were eventually discharged. Their experience indicates that extracorporeal assist devices allow for the safe assistance of patients with isolated or combined heart and lung failure in need of interhospital transfer.

GENERAL SURGERY

Paraumbilical hernia repair during cesarean delivery

Because some pregnant women with paraumbilical hernia request that repair be done at the time of cesarean delivery, Ghnnam and colleagues evaluated the outcome of the combined procedure in a prospective study on 48 patients, comparing them with 100 low-risk patients who underwent cesarean delivery alone. The combined procedure took longer than cesarean delivery alone (75.2 minutes versus 60.5 minutes, $P<.001$), but there were no major complications. Wound infection occurred in six patients (4.1%). Hospital stay did not differ significantly from those of controls. All hernia patients reported that they preferred the combined operation. The combination approach was safe, effective and well accepted.

CARDIOLOGY

Optimal dosing of angiotensin-converting enzyme inhibitors in patients with chronic heart failure: a cross-sectional study in Palestine

In a cross-sectional study, Sweileh and colleagues determined the usage and dosing patterns of ACE inhibitors in CHF patients at a governmental hospital.Of 96 CHF patients receiving an ACE inhibitor, 49 (51%) were receiving an optimal dose and 47 (49%) were receiving a suboptimal dose. Of all patients with CHF and no contraindication (n=138), 88 (64.2%) were either receiving no ACE inhibitor or a suboptimal dose. In the statistical analysis, no valid model could predict the use of an optimal dose. Despite an abundance of evidence in favor of high-dose ACE inhibitor therapy in CHF patients, underutilization and suboptimal dosing were common.

original article

Recurrence of hepatitis C virus genotype-4 infection following orthotopic liver transplantation: natural history and predictors of outcome

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Ann Saudi Med 2009; 29(2): 91-97

BACKGROUND AND OBJECTIVES: There are few reports on hepatitis C virus genotype 4 (HCV-4) recurrences after orthotopic liver transplantation (OLT). Therefore, we undertook a study to determine the epidemiological, clinical and virological characteristics of patients with biopsy-proven recurrent HCV infection and analyzed the factors that influence recurrent disease severity. We also compared disease recurrence and outcomes between HCV-4 and other genotypes.

PATIENTS AND METHODS: All patients who underwent OLT (locally or abroad) for HCV related hepatic cirrhosis from 1991 to 2006 and had recurrent HCV infection were identified. Clinical, laboratory and pathological data before and after OLT were collected and analyzed.

RESULTS: Of 116 patients who underwent OLT for hepatitis C, 46 (39.7%) patients satisfied the criteria of recurrent hepatitis C. Twenty-nine (63%) patients were infected with HCV genotype 4. Mean (SD) for age was 54.9 (10.9) years. Nineteen of the HCV genotype 4 patients (65.5%) were males, 21 (72.4%) received deceased donor grafts, and 7 (24.1%) developed ≥1 acute rejection episodes. Pathologically, 7 (24.1%) and 4 (13.8%) patients had inflammation grade 3-4 and fibrosis stage 3-4, respectively. Follow-up biopsy in 9 (31%) HCV genotype 4 patients showed stable, worse and improved fibrosis stage in 5, 2 and 2 patients, respectively. Of the 7 patients in the recurrent HCV group who died, 6 were infected with genotype 4 and 4 of them died of HCV-related disease.

CONCLUSION: This analysis suggests that HCV recurrence following OLT in HCV-4 patients is not significantly different from its recurrence for other genotypes.

End-stage liver disease secondary to hepatitis C virus (HCV) infection is the major indication for orthotopic liver transplantation (OLT) worldwide.[1] Re-infection of the graft is universal and occurs shortly after transplantation, leading to an accelerated course of liver injury in many cases.[2] Most studies conducted worldwide have investigated disease recurrence in HCV genotypes 1, 2, and 3.[1] However, there are very few reports of post-OLT recurrence of HCV genotype 4 (HCV-4), the predominant genotype in the Middle East.[3-6] Therefore, the aims of this retrospective study were to first, describe the epidemiological, clinical and virological characteristics of all patients diagnosed with biopsy-proven recurrent HCV-4 who were followed at King Faisal Specialist Hospital and Research Center (KFSHRC) in Riyadh, Saudi Arabia; second, determine the host, viral and donor variables that may influence severity of disease recurrence; and finally, compare genotype 4 with other genotypes in terms of epidemiological, clinical and pathological characteristics in addition to disease outcome.

PATIENTS AND METHODS

All patients who received OLT (whether locally or abroad) for liver disease secondary to HCV infection and were followed at King Faisal Specialist Hospital and

Research Centre (KFSHRC), Riyadh, Saudi Arabia, from 1991 through the end of 2006 were identified through a computerized database. The study protocol was approved by the department and the local ethical and research committees. The patient charts, transplant information, and laboratory data were reviewed. Only patients with recurrent HCV infection were included in the analysis. Recurrent hepatitis C was defined as: 1) alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥ 2 times the upper limit of normal; 2) positive HCV RNA polymerase chain reaction (PCR); and 3) liver biopsy consistent with recurrent hepatitis C, with no evidence of graft rejection. Patients were excluded from the study if they had liver biopsy evidence of acute rejection, biliary obstruction, ischemic hepatitis, or any other viral infections. Demographic data, including age and gender of the recipient, type of OLT, donor age, presence and number of acute cellular rejection episodes, viral load pre- and post-transplant, HCV genotype and primary immunosuppressive therapy, were all collected. All patients were followed-up in the post-liver transplant clinic at least every 2 months based on their condition, with regular clinical, biochemical, imaging and virological examinations as appropriate, in addition to the pathological assessment.

HCV detection and quantification were performed using the Abbott Real-Time M2000rt instrument. The HCV assay detects and quantifies genotypes,[1-6] and the Abbott Real-Time HCV assay provides detection limits (analytical measurement range) from 30 to 100 000 000 IU/mL, where 1 IU/mL=4 copies/mL.

Histopathological assessment was performed according to the METAVIR scoring system by a single liver histopathologist.[7] In our center, protocol liver biopsies are not practiced and the decision to perform liver biopsy is made if the serum ALT and/or AST levels are ≥ 2 times the upper limit of normal, or there is a consistent increase in direct bilirubin. The normal reference range of serum ALT and AST in our laboratory is 10-45 IU/L.

Data was collected initially on a specialized data collection form, imported into a Microsoft Excel worksheet and finally transferred to the statistical package for social sciences (SPSS) version 11.0 (SPSS, Chicago, IL, USA) for analysis. Means of continuous variables were compared using the *t* test, non-parametric tests (Wilcoxon and Mann Whitney) or one-way analysis of variance (ANOVA), in addition to the post-hoc test (Tukey) as appropriate. The chi-square or Fisher exact tests were used to compare frequencies and proportions. Multivariate stepwise logistic regression analysis was performed to determine the independent predictors of fibrosis. A *P* value <.05 was considered statistically significant. Cumulative survival was calculated by the life-table method (Kaplan-Meier analysis) from the date of transplantation until the last follow-up, death, or loss of follow-up. Survival of patients in different groups was compared by the log-rank test.

RESULTS

Of the 116 patients who received transplants due to hepatitis C and were followed in our center, 46 satisfied all three inclusion criteria for having recurrent HCV infection post-OLT. Of these 46, 33 (71.7%) were males and the mean (SD) for age was 54.5 (11.2) years. Thirty (65.2%) patients received deceased donor grafts, while 16 (34.8%) received living-related donor grafts. The mean (SD) for donor age was 29.5 (9.8) years and 86% of donors were under the age of 40 years. Twenty-seven patients (58.7%) received transplants at KFSHRC, with the remaining 19 patients receiving transplants abroad, mostly in China, the USA and Germany. Nine (19.9%) patients developed ≥1 episode of acute rejection during follow-up. Clinical, biochemical and virological characteristics of the patients included in our study are shown in Table 1.

At the time of graft biopsy, 14 (30.4%) patients were treated with either tacrolimus or cyclosporine alone, while the remaining 32 (69.6%) received a combination of drugs, mostly either cyclosporine and mycophenolate mofetil (MMF) or tacrolimus and MMF (Table 1). Twenty-six (56.5%) patients were taking steroids at the time of biopsy, and only three (6.5%) received IV steroids for treatment of acute rejection episodes. None of our patients received OKT3 or any other anti-lymphocyte preparation.

Upon initial histological examination, 5 (10.9%) patients had grade 0 inflammation, 10 (21.9%) had grade 1, 21 (45.7%) had grade 2, 8 (17.4%) had grade 3 and 2 (4.3%) had grade 4 inflammation. Fibrosis scoring was performed and showed that 14 (30.4%) patients had fibrosis stage 0, 17 (37.0%) stage 1, 10 (21.7%) were stage 2, 4 (8.7%) were stage 3, and only 1 (2.2%) was stage 4 (cirrhosis). The mean (SD) time between transplant and biopsy was 687.8 (1094.1) days. Seventeen (36%) patients had at least one repeat liver biopsy during the follow-up. Six patients showed worsening fibrosis scores, eight were stable and three improved.

Patients who received OLT at KFSHRC (n=27) were similar to those who had OLT abroad (n=19) in demographic, clinical, biochemical, and virological variables. No significant differences were found between patients who received grafts from living-related donors (n=16) compared with patients who received deceased-

Table 1. Clinical, biochemical and virological characteristics of patients with hepatitis C virus recurrence post-liver transplantation at the time of diagnosis (n=46).

Variable	Mean (SD) or n (%)
Mean recipient age (years)	54.5 (11.2)
Mean donor age (years)	29.5 (9.8)
Sex	
Male	33 (71.7)
Female	13 (28.3)
Type of transplant	
Deceased donor	30 (65.2)
Living donor	16 (34.8)
Transplant site	
KFSH&RC	27 (58.7)
Abroad	19 (41.3)
Rejection	
Yes	9 (19.9)
No	37 (80.1)
Intravenous pulse steroids	
Yes	3 (6.8)
No	43 (93.2)
Mean period on steroids (months)	10.9 (14.3)
Survived	
Yes	38 (82.2)
No	8 (17.8)
Immunosuppression at biopsy time	
Single drug	14 (30.4)
Combination	32 (69.8)
Transplant–biopsy period (days)	687.8 (1094.1)
Positive PCR at time of transplant	45 (97.8)
HCV genotype	
4	29 (63)
Others	17 (37)
Viral load at transplant (million copies/mL)	2.4 (1.8)
Viral load at biopsy (million copies/mL)	1.8 (1.7)
ALT at biopsy (IU/L)	206 (174.3)
AST at biopsy (IU/L)	205.5 (244.2)

ALT: alanine aminotransferase. AST: aspartate aminotransferase. n: number. HCV: hepatitis C virus. KFSHRC: King Faisal Specialist Hospital and Research Centre.

Table 2. Univariable predictors of hepatic fibrosis in patients with recurrent HCV post-liver transplantation (n=46).

Variable	Fibrosis stage 0-1 (n=31)	Fibrosis stage 2-4 (n= 15)	*P*
Sex (M/F)	23 (74.2)/8 (25.8)	10 (66.7)/5 (33.3)	.60
Mean recipient age (≤40/>40 y)	3 (9.7)/28 (90.3)	1 (6.7)/14 (93.3)	.73
Rejection (no/yes)	25 (80.6)/6 (19.4)	12 (80.0)/3 (20.0)	.96
Steatosis in biopsy (no/yes)	20 (64.5)/11 (35.5)	8 (53.3)/7 (46.7)	.47
Mean viral load (low/high)	11 (35.5)/20 (64.5)	1 (6.7)/14 (93.3)	.037*
Transplant type (DDLT/LDLT)	22 (71)/9 (29)	8 (26.7)/7 (46.7)	.24
Transplant site (abroad/KFSHRC)	14 (45.2)/17 (54.8)	5 (33.3)/10 (66.7)	.45
Viral genotype (4/others)	20 (69)/9 (31)	9 (69.2)/4 (30.8)	.99
Steroids (no/yes)	6 (20.7)/23 (79.3)	12 (80.0)/3 (20)	.0001*
MMF (no/yes)	11 (37.9)/18 (62.1)	13 (86.7)/2 (13.3)	.002*

Data are expressed as mean±SD or n (%) as appropriate. MMF: mycophenolate mofitel. LDLT: living donor liver transplantation. DDLT: deceased donor liver transplantation. KFSHRC: King Faisal Specialist Hospital and Research Centre. Viral load low=<40 000 000 copy/mL; high= >40 000 000 copy/mL.

donor grafts (n=30) in demographic, clinical, biochemical and virological variables except for HCV viral load at the time of biopsy, which was significantly higher in patients who received deceased donor grafts (P=.008).

Twenty-nine patients (63.0%) began peginterferon alfa-2a (40 KD; Pegasys, F. Hoffmann-La Roche, Basel, Switzerland) 135-180 mcg per week subcutaneously and ribavirin (Copegus, F. Hoffmann-La Roche, 800-1200 mg per day orally) therapy for 48 weeks based on their initial histological scores (patients were treated if they had elevated ALT of more than 2 times the upper limit of normal and had grade 2 or more inflammation and stage 2 or more fibrosis on liver biopsy. Of these, 16 (55%) were negative for HCV RNA at the end of therapy and three of these 16 (18.8%) relapsed after the end of treatment, resulting in a sustained virological response of 44.8% (13 of 29). After a mean (SD) follow-up of 38.8 (40.8) months (range, 7.9 to 173 months), 4 patients (in addition to the 1 patient who had cirrhosis at the initial liver biopsy) developed cirrhosis; 7 (15.5%) eventually died of liver failure; 1 died of unrelated causes; and the remainder of the patients were still alive at the time of writing.

Of the 46 patients who had recurrent hepatitis C, 29 (63.0%) were infected with genotype 4. Mean (SD) for age was 54.9 (10.9), 19 (65.5%) were males, 21 (72.4%) received deceased donor grafts and 7 (24.1%) developed ≥1 acute rejection episodes. Upon histological examination of liver biopsy samples from these genotype 4 patients (n=29), 4 (13.8%) patients had grade

Table 3. Comparison of HCV genotype 4 and other genotypes in 46 liver transplant recipients with recurrent HCV infection.

Variable	Genotype 4 (n=29)	Other genotypes (n=17)	*P*
Sex (M/F)	19 (65.5)/10 (34.5)	14 (82.4)/3 (17.6)	.21
Mean (SD) age at transplant (years)	54.9 (10.9)	51.7 (12.9)	.41
Donor mean (SD) age (years)	30.6 (10)	25.3 (6.5)	.21
Survival at 12/36 months (%)	88.8/73.6	100/86.7	.30
Death	6 (20.7)	2 (11.8)	.30
Viral load pre-transplant (rank)*	9.9	11.6	.59
Viral load at time of biopsy (rank)*	22.5	19.4	.45
ALT at time of biopsy (IU/L)	179 (148.4)	246 (219.9)	.28
AST at time of biopsy (IU/L)	175 (181.9)	278.7 (257.6)	.54
Mean transplant-biopsy period (days)	786 (1148.3)	532 (1157.1)	.53
Rejection	9 (31.0)	3 (17.6)	.60
Grade 2-4 inflammation	19 (65.5)	12 (70.6)	.46
Stage 2-4 fibroses	9 (31)	6 (35.3)	.99
Diabetes mellitus	17 (58.6)	12 (70.6)	.86
Hypertension	19 (65.5)	6 (35.3)	.04
Hyperlipidemia	1 (3.4)	1 (5.9)	.55

Data are expressed as mean±SD or n (%) as appropriate. SD: standard deviation. ALT: alanine aminotransferase. AST: aspartate aminotransferase. n: number. *Mean rank as calculated by Mann-Whitney test

0 inflammation, 6 (20.7%) had grade 1, 12 (41.4%) had grade 2, 5 (17.2%) had grade 3, and 2 (6.9%) had grade 4 inflammation. Fibrosis scoring showed that 11 (37.9%) patients had fibrosis stage 0, 9 (31.0%) stage 1, 5 (17.2%) were stage 2, 3 (10.3%) were stage 3, and only 1 (3.4%) was stage 4 (cirrhosis). Univariate analysis showed that there was a significant difference between recurrent HCV patients with fibrosis stage ≥2 compared to those with fibrosis stage 0-1 in the viral load at the time of biopsy (P=.04) (Table 2). In addition, there were significant differences in the transplantation-to-biopsy interval (P=.002) and the activity (inflammatory) grade (P=.008). However, multivariate logistic regression analysis of these three variables showed that only the viral load at the time of biopsy was an independent predictor of higher fibrosis stage in patients with HCV-4 recurrence post-OLT (P=.029).

There was no significant difference between patients with HCV-4 and those infected with other genotypes in virological and histological parameters (Table 3). More patients (65.6%) with HCV-4 had hypertension than patients infected with other genotypes (30.8%, P=.036). Seventeen (48%) patients received pegylated interferon and ribavirin therapy, nine of whom responded to therapy and two relapsed after the end of the treatment response, resulting in a sustained virological response of 41%. During 38.5 months of follow-up (range, 7.9-170.5 months), 9 patients had a repeat liver biopsy, 5 showed a stable fibrosis score, 2 showed worsening and 2 showed improvement.

Eight of the 46 patients (17.4%) died during the follow-up. Of those, 6 were infected with HCV-4; of these, 4 died of severe recurrent cholestatic hepatitis C or chronic graft failure secondary to hepatitis C. No significant difference was found between genotype 4 and non-genotype-4 patients in terms of survival during the follow-up period (Figure 1a). Similarly, survival analyses using Kaplan-Meier curves and the log-rank test were similar in the patients who had DDLT and LDLT as well as among those who had OLT locally and abroad (Figure 1b and 1c).

DISCUSSION

Liver disease secondary to HCV infection is the most common indication for OLT worldwide, as well as in Saudi Arabia.[1,8] Whether receiving the transplant locally or abroad, the majority of Saudi patients who receive transplants due to hepatitis C are infected with HCV-4.[9,10] Although HCV genotype has not been shown to affect the natural history of chronic hepatitis C,[11] the effect of genotype following OLT is controversial.[12-14] There are only a few reports describing the natural history of recurrent HCV-4 after OLT in patients infected with genotype 4, most of which are conflicting.[3-6] Gane et al reported on 14 patients with recurrent HCV-4 post-OLT and found that about 50% of these patients have progressive liver disease.[4] Similarly, an analysis of 182 patients transplanted for HCV in Australia and New Zealand (16 of whom had HCV-4) found that, among many factors studied in a univariate and multivariate analyses, genotype 4 was associated with an increased risk for re-transplantation and death.[5] In contrast, a study from another Australian center, including patients with HCV-4, showed that genotype 1b, not 4, was associated with higher recurrence rates after transplant.[6] In a more detailed study from the UK, 32 of 128 patients who underwent OLT for hepatitis C were infected with HCV-4. A statistically significant greater fibrosis progression rate was observed in HCV-4 patients compared to non-genotype-4 ones, although their rates of survival were similar.[3] The authors attributed the difference between these two groups to the significantly older donor age in the HCV-4 group and the ethnic background of these patients (predominantly Egyptian). They stated that: "donor livers that were suitable for transplantation but unsuitable or not needed for citizens of the United Kingdom (UK) were offered to non-UK citizens who formed a second waiting list."[3] This policy may have led to the selection of inferior grafts for HCV-4 patients, who are predominantly non-UK citizens, leading to inferior results in these patients. When reporting the histological findings, these investigators used the last available scored biopsy (showing significantly higher fibrosis progression rates). However, they did not report the findings of the initial liver biopsy, which was done according to a day-six protocol. It would have been interesting to see if indeed the quality of grafts given to patients with HCV-4 was inferior to that of those given to other patients.

In the current study, we report the results of patients who have biopsy-proven recurrent hepatitis C infection and make comparisons between patients with HCV-4 and non-HCV-4 genotype. Contrary to previous reports, our study showed that there were no significant differences between these two groups in terms of epidemiological, clinical and histological factors and outcome. We found that in the initial liver biopsy, which was performed after a mean time from transplantation of more than 2 years, there were only four patients who had fibrosis scores greater than stage 3. Two of these patients had worsening fibrosis on subsequent biopsies.

Although the majority of deaths in our study were in genotype-4 patients (6 of 8 deaths), there were only 4 hepatitis C virus-related deaths in the HCV-4-infected patients (13% mortality) after a mean (SD) of 14.7 (6.6) months of follow-up and we found no statistical difference in survival between genotype-4 patients and patients infected with other genotypes. The relatively good results seen in our HCV-4 patients (44.8% sustained viral response) may be explained by a number of factors. First, donor selection tends to be extremely conservative in our center, as marginal livers are very frequently rejected. Second, our mean donor age (about 30 years), an important parameter in post-transplant outcome, especially in hepatitis C patients, is significantly lower than what has been described in other studies.[15,16] Third, only 6.8% of patients used IV steroids, and none used anti-lymphocyte preparations. Fourth, the HCV mean viral load at the time of transplant seems to be lower in our study compared to previously reported studies on the same genotype. Fifth, we based this analysis on the initial liver biopsy with the first elevation of liver en-

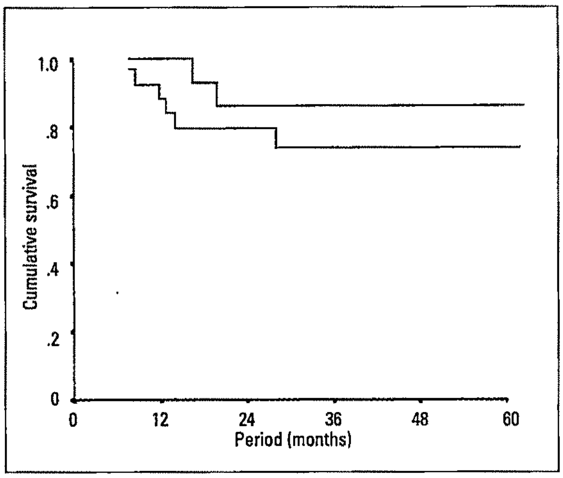

Figure 1a. Kaplan-Meier survival analysis in genotype-4 patients (green) versus those with other genotypes (blue), *P*=.297 by log-rank test.

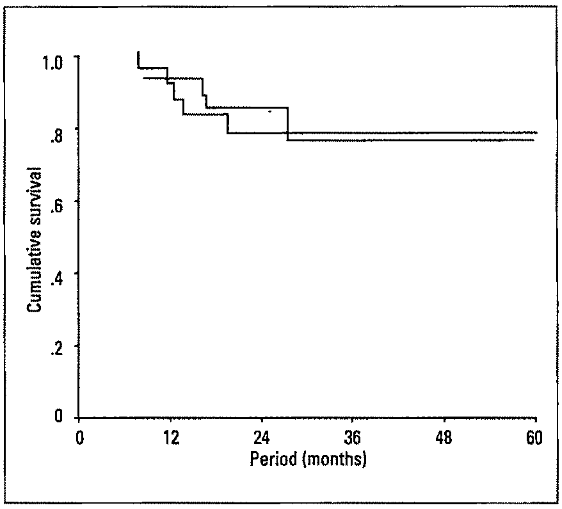

Figure 1b. Kaplan-Meier survival analysis in patients who received transplantation locally (blue) versus those who were transplanted abroad (green), *P*=.869 by log-rank test.

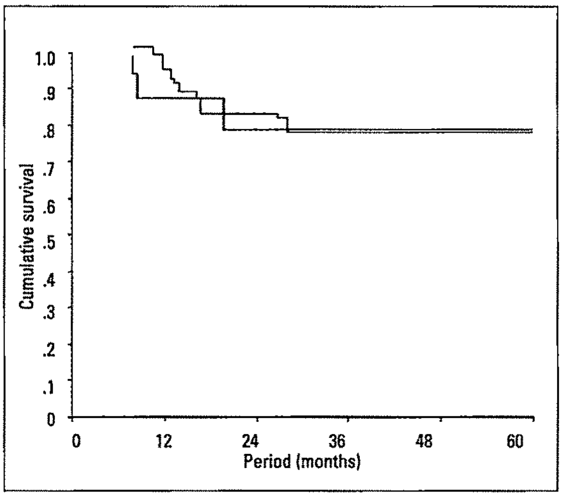

Figure 1c. Kaplan-Meier survival analysis in patients who received DDLT (blue) versus those who received LDLT (green), *P*= .778 by log-rank test.

zymes, although the mean time from transplantation to initial biopsy was more than 650 days. Among many factors included in our analyses, the only factor predictive of an advanced histological score was the HCV RNA level at the time of biopsy. Although some studies have shown a positive correlation between pre-transplant viral load and severity of HCV recurrence after transplantation,[17,18] others have not shown a consistent correlation between HCV viral load post-liver transplant and histological outcome.[12,13] Our data suggest that this correlation may be important in at least genotype-4 patients. This is also supported by the fact that all patients who received antiviral therapy and responded to it had either stable or improved histological scores. Recently, treatment of hepatitis C post-OLT has been shown to improve survival in such patients, further suggesting a correlation between viral load and severity of disease.[19]

The main strength of the present study is that it included patients who had transplantation locally in our center as well as patients who received transplantations abroad. In addition, it included patients who received deceased donor and living related grafts. It also included patients with genotype 4 of an ethnic background different from the one described in most previous studies reporting on genotype-4 patients (Saudi and Egyptian patients). All these factors gave a wider variety of genotype-4 patients, which allows study of this genotype in a more comprehensive fashion. Additionally, this study had a long follow-up time.

The outcome of recurrent HCV-4 appears to be not affected by the type of liver OLT (LDLT or DDLT). This may emphasize a greater role for host, viral, donor and therapeutic variables on disease severity. Although this is an issue that generated some debate recently, a recent study by Lawal et al[20] showed no difference in the cumulative incidence of histological recurrence of HCV post-OLT or in the survival between recipients of DDLT (n=32) and those with split liver transplants (n=17), which is consistent with our results. The same result was also shown by a retrospective study involving 289 HCV patients, which concluded that LDLT does not increase HCV recurrence and progression.[21] However, both studies[20,21] came from areas where genotype 1 infection predominates. Further studies are needed to assess the role of transplant type on the severity of recurrent HCV-4.

Our study suffers from all the weaknesses inherent to a retrospective analysis. In addition, because we have not been practicing protocol biopsy in our center, it was extremely hard to draw strong conclusions from the fibrosis progression results we have reported. In conclusion, our study suggests that HCV recurrence post-OLT in genotype-4 patients does not seem significantly different from recurrence in other genotypes.

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original article

The reliability and validity of the short version of the WHO Quality of Life Instrument in an Arab general population

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The English and other versions of the WHO Quality of Life-BREF are available online: *http://www.who.int/substance_abuse/research_tools/whoqolbref/en/*. The Arabic version is part of the electronic version of this article available on *http://www.saudiannals.net*

Ann Saudi Med 2009; 29(2): 98-104

BACKGROUND AND OBJECTIVES: There is rising interest in quality of life (QOL) research in Arabian countries. The aim of this study was to assess in a nationwide sample of Kuwaiti subjects the reliability and validity of the World Health Organization Quality of Life (WHOQOL-BREF), a shorter version of the widely used QOL assessment instrument that comprises 26 items in the domains of physical health, psychological health, social relationships, and the environment.

METHODS: A one-in-three systematic random proportionate sample of consenting Kuwaiti nationals attending large cooperative stores and municipal government offices in the six governorates completed the Arabic translation of the questionnaire. The indices assessed included test-retest reliability, internal consistency, item internal consistency (IIC), item discriminant validity (IDV), known-groups and construct validity.

RESULTS: There were 3303 participants (44.8% males, 55.2% females, mean age 35.4 years, range 16 to 87 years). The intra-class correlation for the test-retest statistic and the internal consistency values for the full questionnaire and the domains had a Cronbach's alpha$\geq$0.7. Of the 24 items that constitute the domains, 21 met the IIC requirement of correlation $\geq$0.4 with the corresponding domain, while 16 met the IDV criterion of having a higher correlation with their corresponding domain than other domains. Domain scores discriminated significantly between well and sick groups. In the factor analysis, four strong factors emerged with the same construct as in the WHO report.

CONCLUSION: The Arabic translation of the WHOQOL-BREF has impressive reliability and validity indices. The poor IDV findings are due to the multidimensional nature of the questionnaire. The highly significant validity indices should reassure researchers that the questionnaire represents the same constructs across cultures. Negatively worded items possibly need refinement.

Recent interest in quality of life (QOL) as an outcome measure in medicine has inspired studies in chronic medical[1-3] and general population subjects[4,5] in Arab and neighboring countries. To further this interest, it is important to use assessment instruments that are psychometrically sound and have cross-cultural validity, so as to make findings comparable across countries. In this regard, the short version of the World Health Organization's QOL Instrument, the WHOQOL-BREF,[6] is of interest for the following reasons: First, it was simultaneously developed in diverse cultures, thus overcoming the usual controversy over the problem of applying a questionnaire articulated in one culture in a different culture.[7] This means that the instrument has a strong potential for easy cross-cultural applicability, since the items are framed in culture-neutral terminology. Second, the items include widely valued contextual factors of life that are not generally regarded as health-related.[8] Therefore, it is a generic instrument that assesses health-related QOL (HRQOL), and social, environmental and subjective well-being issues.

The Arabic translation of the WHOQOL-BREF has been shown to have highly significant structural integrity characteristics.[9] The Persian translation has been shown to have significant values for some reliability and validity indices.[4] In this study, we sought to contribute to published data on the Arab population by sampling Kuwaiti subjects. Our specific objectives were to assess the following reliability and validity indices, in comparison with the WHO 23-country report:[6]

(i) the test-retest reliability of the WHOQOL-BREF; (ii) the floor/ceiling effect and acceptability of the WHOQOL-BREF, as well as the internal consistency of the full questionnaire and its constituent four domains of QOL; (iii) the item-internal consistency (IIC) and item-discriminant validity (IDV);[10] (iv) the construct validity by exploratory factor analysis, and known-groups validity by analyzing the differences in domain scores between sick and well subjects. Based on published information,[4,6,9] we hypothesized that the reliability and validity indices in an Arab population would be consistent with these indices in other populations. Furthermore, all domains were expected to be strongly and positively correlated with the concept of overall QOL and health (i.e., general facet on health and QOL).[6]

METHODS

Of the 3.4 million population of Kuwait, Kuwaiti nationals make up 1.1 million (48.9% male, 51.1% female) (2007 census). About 97% live in urban areas. The adult literacy rate in Arabic is 83.5% (2003 estimate) and the unemployment rate is 2.3% (2004 estimate by the Kuwait Public Authority for Civil Information). Administratively, the country is divided into six governorates, each consisting of a centrally located large cooperative supermarket store, as well as municipal government and immigration offices. Our sampling framework was the six governorates, and participants were recruited at the above locations. Our sample size was guided by the recommendation of the International Quality of Life Assessment (IQOLA) project researchers, that the sample size for general population norming should be 2500-3000.[10]

We obtained census data for each governorate from the Public Authority for Civil Information. Using quota sampling, we generated the number of potential participants that would constitute a proportionate representation of governorates, by gender, for a sample size of at least 3000 subjects. Although Kuwait has the infrastructure for generating a sampling framework for a representative general population study (e.g. telephone listing, voting register), the strict conservative culture makes it impossible to carry out house-to-house surveys for private studies such as ours. To overcome this obstacle, researchers have attempted to target people that visit popular government administrative offices (e.g. municipal government and immigration offices) and the large cooperative shops. In a recent Kuwaiti study,[11] it was found that the large cooperative shops constituted convenient venues for interviewing women in traditional social roles who are not represented in the work force. In a study comparing the attitudes towards women in Kuwait and Qatar, Abdalla[12] overcame the difficulty of house-to-house surveys by interviewing respondents in their work places.

To obtain a fairly representative national sample, we used the above methodologies to sample prospective respondents in these popularly accessed facilities of each of the governorates. This sampling methodology is feasible in Kuwait because of the small population, the urban residence, and the favorable education and employment circumstances. Hence, it is reasonable to assume that a fairly representative proportion of Kuwaiti nationals patronize the above popular urban places, and that they are literate enough in Arabic to complete uncomplicated questionnaires on their own.[11]

For the operational definition of QOL we accepted the WHO definition as the individuals' perception of life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards and concerns.[6] The measure focused on subjective QOL, as distinct from objective QOL.[13]

The WHOQOL-BREF

The WHOQOL-BREF is a 26-item, self-administered, generic questionnaire that is a short version of the WHOQOL-100 scale.[6] The response options range from 1 (very dissatisfied/very poor) to 5 (very satisfied/very good). Assessments are made over the preceding two weeks. It consists of domains and facets (or sub-domains). The items on "overall rating of QOL" (OQOL) and subjective satisfaction with health constitute the general facet on OQOL and health. The more popular model for interpreting the scores has four domains, namely, physical health (seven items), psychological health (six items), social relations (three items) and environment (eight items). Our analysis was based on this model. The domain scores of the WHOQOL-BREF can be computed in three ways. The first is a summation of the raw scores of the constituent items. The second and third ways consist of transforming the raw scores. In the second way, the raw scores are transformed into scores that range from 4-20, to be in line with the WHOQL-100 Instrument. The third way converts the 4-20 scores onto a 0-100% scale.[14]

Data collection

The study took place in 2006-2007. The questionnaire was translated into Arabic by the method of back-translation. Ethical approval for the study was obtained from Kuwait University and the Kuwait Foundation for the Advancement of Science (KFAS). We obtained permission from the authorities of each study location to interview Kuwaiti nationals attending their facility. All participants gave verbal informed consent. The staff of a professional social research company was responsible for circulating and retrieving the questionnaires. These research assistants (RAs) were all Kuwaiti nationals, aged 21 to 27 years, who had previously undergone a 2-month course on research methods and interview techniques at Kuwait University. Pairs of RAs (one male, one female) worked in their own governorates of residence, so that they were familiar with the cultural environment. As a rule, prospective female respondents were approached by a female RA. To recruit prospective respondents, the RAs were positioned at the main entrance of a place, introduced themselves as Kuwaitis doing a research, and politely asked the nationality of the prospective participant. This was to ensure that only Kuwaiti nationals were recruited. Thereafter, the objectives of the study were explained and the subject was informed that no penalty would result from declining to participate. We used a systematic random sampling of one-in-three subjects (by gender). If a subject declined to participate, the next third person was approached. We continued in this way until we reached the population quota for the governorate. At the preliminary stage of the study, the RAs were trained in the use of the study's questionnaires in a one-week period. We did not compute inter-rater reliability because the questionnaires were all administered as self-report. Only subjects literate in Arabic were invited to participate. In all cases, the participants completed the questionnaire anonymously and privately. The RAs were nearby to offer assistance in clarifying the items. All subjects completed the Arabic translation of the questionnaire. Test-retest reliability was done by giving the questionnaire twice in a one-week period to 50 subjects who did not participate in the main study.

Data analysis

Data were analyzed by SPSS version 11 (SPSS Inc, Chicago, Illinois). QOL domain scores (range, 4-20 and 0% to 100%) were generated by organizing the items into the four domains as recommended.[6] Data for test-retest reliability were analyzed by intra-class correlation coefficient (ICC). The internal consistency for the full questionnaire and domains was assessed by Cronbach's alpha for the 3303 participants, with a recommended cut-off value of ≥0.7. The acceptability of the questionnaire was assessed by the missing values or proportion of respondents who failed to complete each item. A cut-off value of <2.5% is recommended for each item.[10] The proportion of respondents scoring at the lowest level (floor effect) and the highest level (ceiling effect) for each item was assessed. This is a measure of sensitivity to change and how far the item can be assumed to be capturing the full range of potential responses in the population.[10] Item internal consistency (IIC) and item discriminant validity (IDV), measured by the Pearson correlation, were assessed after controlling for item overlap in the corresponding scale. The IIC and IDV concern the relationship of each item to its hypothesized scale or domain. The IIC rule requires that the item should correlate r ≥0.4 with its adjusted scale score. For IDV, the item should have the highest correlation with its scale, in comparison with other scales in the questionnaire.[10]

The construct validity of the WHOQOL-BREF was assessed by exploratory factor analysis, using principal components analysis with orthogonal rotation for factors that have Eigen values above 1.[6] Known-groups validity was assessed by testing the significant differences in domain scores between subjects who rated themselves as being well and those who rated themselves as being sick, using standardized effect size calculations. The relationship between the general facet and the domains was assessed by the Pearson correlation. Missing data were handled by excluding cases analysis by analysis. The level of statistical significance was set at 5%, and all tests were two-tailed.

RESULTS

Socio-demographic characteristics

Of the 3376 subjects who agreed to participate in the study, 73 questionnaires were voided because subjects did not complete over 20% of the items of the WHOQOL-BREF, as recommended by the WHOQOL Group.[6] Hence we report data for 3303 subjects. The 3303 participants consisted of 44.8% (n=1479) men and 55.2% (n=1824) women, aged 16 to 87 years with a mean (SD) of 35.4 (11.9) years, with a proportionate representation of the six governorates. As in the Kuwaiti national general population, women were in the majority and 2.4% of the subjects were 65 years of age or older. The subjects were predominantly educated (59.9% had at least college education), employed in skilled work (58.4%), and married (60.8%).

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Table 1. Internal consistency of the WHOQOL-BREF for all participants, and test-retest reliability for non-participating subjects.

Questionnaire/domain QOL	No. of items	Cronbach's alpha	Split-half reliability
Internal consistency:			
WHOQOL-BREF (n=3303)	26	0.93	0.89
Physical health domain WHOQOL-BREF	7	0.80	
Psychological health domain	6	0.77	
Social relations domain	3	0.69	
Environment domain	8	0.83	
Test-retest reliability	26×2	(95% C.I.)*	
WHOQOL-BREF (n=50)		0.95 (0.94-0.97)	

*Intra-class correlation coefficient and 95% confidence interval.

Descriptive statistics and internal consistency

The ICC for the test-retest statistic (0.95) was highly significant. Similarly, the internal consistency values for the full questionnaire and the domains met the 0.7 Cronbach's alpha value requirement (Table 1). With the exception of the item on sexual satisfaction (7.9%), the proportion of missing values ranged from 0.06% to <1% for 18 items, and from 1% to 1.8% for seven items. This shows that the contents of the questionnaire were generally acceptable to the respondents. Our rate of missing values for the item on sexual satisfaction is comparable to the 6.0% reported by the WHO, but higher than the 2.5% reported from Iran[4] where the questionnaire was interviewer-administered. The mean (SD) scores for the items ranged from 3.39 (1.2) to 3.89 (0.99) for 23 items; it was 4.0 (1.1) for two items (mobility and transport), and 2.96 (0.98) for one item (negative feelings). With regard to the floor and ceiling effects, the total frequency of lowest scores was 4.7% (range, 2.2% to 8.9%), while the total frequency of highest scores was 24.9% (range, 6.8% to 42.2%). The comparable figures for the WHO report were 4.0% (range, 1.7% to 8.8%) and 17.5% (range, 10.1% to 35.2%), respectively.[6]

Item internal consistency and item discriminant validity

Of the 24 items that constitute the domains, 21 met the IIC requirement of correlation ≥0.4 (Table 2). Only the three negatively worded items (on pain, need for medical treatment and negative feelings) did not meet this requirement. However, these three items were among the 16 that met the IDV criterion of having a higher correlation with their corresponding domain more than other domains. Two more items had equal correlation with at least one more domain other than their corresponding domain. In the WHO 23-country report,[6] it was noted that in 7 of 24 centers, the items on pain and the need for medical treatment were generally problematic in item-total correlations in the physical domain. In addition, poor item-total correlation (<0.3) was noted for negative feelings in one center.

Construct validity: factor analysis

In factor analysis with all the 26 items, four strong factors (i.e., each with >3 items) and one weak factor (with 3 items) emerged, accounting for 58.7% of the variance. Each item loaded highly (≥0.45) on the corresponding factor (Table 3). Interestingly, the four strong factors emerged exactly in the same sequence and with the same construct as in the WHO report. The three negatively worded items constituted the fifth factor. Of the 8 items in Factor I, five belong to the original physical health domain. It is noteworthy that the two general facet items (representing subjective well-being) were in this factor. Factor II is conceptually similar to the original psychological health domain because, of the five constituent items, three belong to psychological health. Factor III is conceptually similar to the original social relations domain because it contains the three items that define that domain. Factor IV appears to be a tighter definition of the environment domain because all the seven items were derived from that domain.

Known-groups validity and the relationship of domains with the general facet

Using the 0-100 scale scores in effect size calculations (effect size, 95% confidence interval), we found that those who rated themselves as being well had significantly higher scores in all domains: physical health (0.50, 0.43-0.57), psychological health (0.36, 0.29-0.44), social relations (0.31, 0.24-0.38) and environment (0.30, 0.23-0.38) domains ($P<.0001$). Finally, the general

Table 2. Item-internal consistency and item-discriminant validity: WHOQOL-Bref: Pearson's r ≥0.4*

WHOQOL items arranged by 4 domains	Physical health	Psychological health	Social relations	Environment
Physical health**				
Pain prevents activities	0.34	0.17	0.08	0.11
Enough energy for daily life	0.60	0.64	0.49	0.59
Able to get around	0.62	0.51	0.46	0.51
Satisfaction with sleep	0.57	0.54	0.49	0.56
Satisfaction with ADL	0.69	0.61	0.53	0.59
Satisfaction with work capacity	0.59	0.55	0.52	0.51
Need treatment to function	0.39	0.19	0.14	0.16
Psychological health				
How much enjoy life	0.48	0.63	0.47	0.59
Feel life meaningful	0.43	0.63	0.47	0.56
Able to concentrate	0.46	0.53	0.42	0.53
Accept bodily appearance	0.49	0.46	0.38	0.49
Satisfaction with self	0.59	0.58	0.63	0.59
How often negative feelings	0.26	0.27	0.22	0.26
Social relations				
Satisfaction with personal relationships	0.48	0.58	0.57	0.55
Satisfaction with sex life	0.45	0.49	0.45	0.44
Satisfaction with friends' support	0.39	0.44	0.49	0.52
Environment				
Feel safe in daily life	0.48	0.63	0.48	0.59
Healthy physical environment	0.40	0.59	0.45	0.59
Have enough money for needs	0.42	0.53	0.41	0.58
Satisfaction information for day-to-day life	0.46	0.53	0.41	0.56
Have leisure opportunity	0.39	0.44	0.35	0.46
Satisfaction living place	0.45	0.51	0.54	0.59
Satisfaction with access to health service	0.35	0.34	0.36	0.49
Satisfaction with transport	0.43	0.42	0.44	0.53

*Corrected for overlap of items in domain **Items in bold belong to the corresponding domain

facet score was highly significantly correlated with the scores for all the domains: physical health (r=0.63), psychological health (r=0.66), social relations (r=0.53) and environment (r=0.61) domains (*P*<.0001).

DISCUSSION

A major limitation of the study is that the subjects were not a representative house-to-house sample of the general population. In particular, those who did not attend the study locations were not represented. This limitation is inherent in the socio-cultural circumstances of the country.[11,12] In view of this limitation, it was not practically possible to keep track of the number of refusals and their characteristics. However, it is reasonable to assume that our nationwide sample had adequate characteristics to estimate the psychometric properties

Table 3. Factor analysis using all 26 items of the WHOQOL-Bref.

Factor label	Items of WHOQOL-Bref	Item loading	Eigen value	% Variance	Total variance
Factor I: General physical health and overall QOL	Ability to get around	0.71	10.2	39.1	58.7
	Energy for life	0.66			
	Satisfaction with general health	0.58			
	Satisfaction with work capacity	0.56			
	Accept bodily appearance	0.54			
	Activities of daily living	0.54			
	Overall rating of QOL	0.49			
	Satisfaction with sleep	0.46			
Factor II: Psychological Health	Feel life meaningful	0.67	1.7	6.6	
	Enjoyment of life	0.67			
	Physical environment health	0.65			
	Feel safe in daily life	0.65			
	Able to concentrate	0.52			
Factor III: Social relations	Satisfaction with personal relations	0.68	1.2	4.7	
	Satisfaction with sex	0.64			
	Satisfaction with self	0.63			
	Satisfaction with support from friends	0.58			
Factor IV: Environment	Satisfaction with access to health service	0.73	1.2	4.5	
	Satisfaction with transport	0.57			
	Enough money for needs	0.56			
	Satisfaction with condition of place of living	0.53			
	Opportunity for leisure activities	0.48			
	Satisfaction with available information	0.47			
Factor V: Health care needs	Pain	0.86	1.0	3.9	
	Need for medical treatment	0.79			
	Negative feelings	0.52			

Kaiser-Meyer-Olkin measure of sampling adequacy=0.95

of the WHOQOL-BREF.[10]

In line with the hypothesis that the reliability and validity indices are similar to those in other populations, the Arabic translation of the WHOQOL-BREF generally met the statistical criteria for the reliability issues investigated. In particular, our findings were similar to those of the WHO 23-country report.[6] There are three notable discrepancies: the relatively high proportion of missing values for the item on sexual satisfaction, the failure of the three negatively worded items to meet the IIC requirement, and the fact that only 16 items met the IDV requirement. A relatively minor discrepancy is the fact that the alpha coefficient for the social relations domain (0.69) was just short of the 0.7 mark. These discrepancies are well known in the literature. The sexual item is usually a problem, where respondents complete the questionnaire on their own, as in our study. In a Taiwanese study, the rate of missing values ranged from 0.9% to 7.7%.[15] In general population studies from Poland and Iran, only the social relations domain failed to meet the required value for internal consistency.[4,16] This problem is related to the fact that the domain has only three items.

We could not attribute the poor IIC performance of the three negatively worded items to translation problems because they met the IDV requirement and the problem was also evident in some centers in the WHO report. Furthermore, the items loaded very highly (>0.5) in the factor analysis. The issue of poor performance in IIC and IDV has been noted in other ways by studies that used the Rasch and item response theory models,[17,18] and is attributable to the multidimensional nature of the instrument.[18]

Our most impressive findings were for construct and known-groups validity. Our first four factors are a fair representation of the original WHO data[6] and have been replicated by others.[19,20] In a Sudanese study, the following factors were replicated: social relations, environment, and the small factor containing the three negatively worded items. Furthermore, in confirmatory factor analysis, the four-domain model had the best fit indices.[9] Our results thus support the impression that the same perceptions of the WHOQOL-BREF are found across cultures and disease conditions,[19] a cardinal requirement for a cross-culturally useful questionnaire. Furthermore, the two general facet items loaded highly on Factor I. This indicates the importance of the general facet as a first deconstruct of the QOL construct,[21] and hence it is a fair representation of the idea of global QOL/ subjective well-being.[22,23] In support of this point, the general facet was highly significantly correlated with the four domains.[6]

In conclusion, the Arabic translation of the WHOQOL-BREF has high reliability and validity indices. It represents the same constructs across cultures.[19] Our validity data support the impression that the WHOQOL-BREF is a cross-culturally valid generic instrument that is composed of parts that address the main issues of the subjective QOL construct in medicine, namely HRQOL, contextual issues and subjective well-being.[8] A possible area need further development is the phrasing of negatively worded items, perhaps by having them rated in a positive direction as the other items.

Acknowledgments

The project was carried out with a grant from the Kuwait Foundation for the Advancement of Sciences (KFAS). Joy Wilson coded all the data. Charles Osuagwu played an invaluable role in locating literature. The staff of Al-Bayan for Translation was responsible for administering the questionnaire in the community. Dr Yusuf Al-Failakiya coordinated the work in the community. We thank the staff and heads of administration and the participants at the various locations in the community where the study took place.

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original article

Management of traumatic brachial artery injuries: A report on 49 patients

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Ann Saudi Med 2009; 29(2): 105-109

BACKGROUND AND OBJECTIVE: The brachial artery is the most frequently injured artery in the upper extremity due to its vulnerability. The purpose of our study was to review our experience with brachial artery injuries over a 9-year period, describing the type of injury, surgical procedures, complications, and associated injuries.

PATIENTS AND METHODS: Forty-nine patients with brachial artery injury underwent surgical repair procedures at our hospital, from the beginning of May 1999 to the end of June 2008. The brachial artery injuries were diagnosed by physical examination and Doppler ultrasonography. Depending on the mode of presentation, patients were either taken immediately to the operating room for bleeding control and vascular repair or were assessed by preoperative duplex ultrasonography.

RESULTS: This study group consisted of 43 males and 6 females, ranging in age from 6 to 65 years with a mean (SD) age of 27.9 (6.7) years. The mechanism of trauma was penetrating in 45 patients and blunt in the remaining 4 patients. Stab injury was the most frequent form of penetrating trauma (24 of 45). Treatment included primary arterial repair in 5 cases, end-to-end anastomosis in 28 cases, interposition vein graft in 15 cases, and interposition-ringed polytetrafluoroethylene graft in 1 case. Associated injuries were common and included venous injury (14), bone fracture (5), and peripheral nerve injury (11). Fifteen patients developed postoperative complications. One patient underwent an above-elbow amputation.

CONCLUSIONS: Prompt and appropriate management of the brachial artery injuries, attention to associated injuries, and a readiness to revise the vascular repair early in the event of failure will maximize patient survival and upper extremity salvage.

Upper extremity arterial trauma may significantly impact the outcome of the trauma patient, but the literature regarding this topic is scarce. Although relatively uncommon, injuries to the arteries of the upper extremity are serious and have the potential to significantly impact the outcome of the trauma patient.[1] The brachial artery is the most frequently injured artery in the upper extremity. Its injury accounts for approximately 28% of all vascular injuries.[2] The degree of ischemia after brachial artery injuries depends on whether the injury is proximal or distal to the profunda brachii.[3]

All brachial artery injuries can be managed successfully unless associated with severe concomitant damage to nerves. The median nerve courses with the brachial artery throughout its length. The radial and ulnar nerves parallel portions of the brachial artery. Therefore, as in all upper extremity vascular injuries, there is a high incidence of associated nerve injuries with brachial artery injuries.[3] The purpose of our study was to review our experience with brachial artery injuries over a 9-year period. The type of injury, surgical procedures, complications, and associated injuries were reviewed.

PATIENTS AND METHODS

Forty-nine patients with brachial artery injury underwent surgical repair procedures at our hospital from the beginning of May 1999 to the end of June 2008. The brachial artery injuries were diagnosed by physical examination and Doppler ultrasonography. The following findings were considered to be signs of arterial injury: brisk bleeding, expanding pulsatile hematoma, pale and cold upper extremities, absent or weak radial and ulnar pulses and associated profound neurological deficits. In this series, an average brachial-brachial Doppler index less than 0.5 was considered diagnostic for brachial artery injury. The initial management of the patients was conducted according to the principles of the advanced trauma and life support (ATLS) guidelines for trauma management.[4] For patients presenting with hard signs of penetrating vascular injury, prompt surgical intervention without further diagnostic evaluation was used. Patients with blunt arterial injury or with penetrating injuries with clinical soft signs (cod extremity, color change, nonexpanding hematoma) underwent plain upper extremity radiography and Doppler ultrasonography (Figure 1).

The indications for fasciotomy were clinically evident or impending compartment syndrome, massive swelling in the upper limb, ischemia lasting more than 6 hours and any motor or sensory deficits. In all patients with associated bone fracture, vascular repair always preceded orthopedic reconstruction. Endoluminal shunts were not required in any of the patients. Successful repair was assessed by the return of radial and ulnar pulses at the end of the operation.

Patients with more severe soft tissue and muscle injuries were treated with thorough debridement of all grossly nonviable tissue, with removal of foreign bodies and copious irrigation with isotonic saline solution, and then injured vessels were exposed. Heparin was administered intravenously for systemic anticoagulation before the vessels were clamped proximally and distally with nontraumatic vascular clamps. Fogarty catheters were used for thrombectomy of the distal and proximal arterial segments. All patients received intravenous heparin for a period of 5-7 days postoperatively and were discharged home on oral aspirin 100 mg/day for a period of 3 months.

Exposure of the brachial artery in the arm was always approached with a median incision in the line of the sulcus separating the biceps muscle from the triceps muscle. The median nerve was always identified and separated from the brachial artery. Exposure of the artery at the elbow was performed with a skin crease incision made at the elbow, with longitudinal extensions along the line of the brachial artery medially and down the brachioradialis laterally. Primary arterial repair or end-to-end anastomosis was preferred whenever possible; otherwise, the interposition saphenous vein graft was used (Figure 2).

All associated brachial venous injuries except one were repaired, in an attempt to prevent postoperative venous hypertension and to minimize development of compartment syndrome. Associated nerve injuries were repaired whenever possible. Repaired vessels, especially at the anastomotic suture lines and graft location, were compulsorily covered with muscles and soft tissue to prevent desiccation and disruption. All patients received intravenous prophylactic antibiotics, which were continued postoperatively for 3 to 5 days, unless prolonged use was dictated by the presence of contamination or infection.

One month after hospital discharge, patients were routinely examined in the outpatient department where segmental pressures were measured and functional status of the upper extremity assessed. Thereafter, they were followed at 3-month periods.

Statistical analysis was performed using the paired samples t test to determine whether there was any statistically significant difference between preoperative and postoperative Doppler pressure indices. A *P* value of less than .05 was taken to indicate significance.

RESULTS

This study group consisted of 43 males and 6 females, ranging in age from 6 to 65 years with a mean (SD) age of 27.9 (6.7) years. The right upper limb was the more frequently affected side as it was involved in 28 patients and the left side in 21 patients. The mechanism of trauma was penetrating in 45 patients and blunt in the remaining 4 patients (from road traffic accidents). Stab injury was the most frequent form of penetrating trauma (24 of 45). Other forms of penetrating trauma in a descending order of frequency were window glass injuries in 11 patients, gunshot injuries in 9 patients, and industrial accident in 1 patient. Thirty-four patients presented with hemorrhage, 28 with ischemia, 8 with hematoma and 1 with a pseudoaneurysm (Table 1).

In 42 patients the diagnosis of arterial injury was based on clinical and hand-held Doppler examination. Preoperative duplex scan was used in only 7 patients. Physical examination and Doppler ultrasonography revealed the absence of arterial pulses in 43 patients and weak arterial pulses in 6. For brachial artery injuries the average brachial-brachial Doppler pressure index was 0.434 (0.046), (range, 0.23 to 0.48) preoperatively, and 0.894 (0.031) (range, 0.83 to 0.93) postoperatively ($P<.05$). Treatment included primary arterial repair in 5 cases, end-to-end anastomosis in 28 cases, interposition vein graft in 15 cases and interposition ringed PTFE graft in 1 case. There were 14 patients with associated brachial vein injury, of which 4 cases had primary repair, 8 had end-to-end anastomosis and 1 had saphenous vein graft interposition. One severely injured brachial vein was compulsory ligated. Five of the 49 patients had injuries to bony structures. Fractures occurred most frequently among patients with blunt trauma (3 patients); fracture was also detected in 2 patients with gunshot wound. All fractures were treated with external fixation.

Eight patients had tendinous injuries that were repaired perioperatively by orthopedic surgeons. Additionally, fasciotomy was performed in 6 patients.

Eleven of 49 patients had peripheral nerve injury: 2 had injuries to the median and ulnar nerves, 6 had injuries to the median nerve alone and 3 had injuries to the ulnar nerve alone. Eight of the 11 nerve injury cases were primarily repaired perioperatively by neurosurgeons. Postoperatively, all patients with nerve injury underwent electromyelography for evaluation of nerve deficit. During the follow-up period, functional recovery was achieved in 6 of these patients. In the remaining patients, functional disability was evident throughout follow-up period. They were followed up neurosurgery and rehabilitation clinics.

Fifteen patients developed postoperative complications consisting of wound infection (2 patients), permanent nerve damage (4 patients), ischemic symptoms due to graft thrombosis (4 patients) and thrombosis of the venous repair (5 patients). Amputation was required in one patient who was involved in a traffic accident and suffered from a proximal brachial artery laceration with injuries to the brachial vein, and the median and ulnar nerves above the elbow in association with a fracture of the humerus. He was operated on 10 hours after injury. Arterial flow was reestablished successfully with a saphenous vein bypass graft and the brachial vein was ligated, but subsequent above-elbow amputation was required due the severity of concomitant nerve and bony injuries with a nonfunctional right upper limb and infection. Two patients with blunt trauma experienced wound infections, but these infections were resolved within 15 days by antibiotic therapy. Four patients experienced early postoperative graft thrombosis. In these patients, thrombectomy was performed. It was successful in three patients. Although thrombectomy was unsuccessful in the remaining one patient with prosthetic graft interposition, amputation of the limb was not required due to adequate collateral circulation.

Postoperatively, all patients who had brachial vein injury experienced various degrees of edema in the upper extremity. This edema decreased with elevation in all patients during the follow-up period (approximately 15 to 45 days). Postoperative venous Doppler studies showed thrombosed repair in five cases without any complication. No patients expired and 48 patients were discharged home with good functional vascular status and limitations based on the degree of associated nerve injury.

The average follow-up period was 20 months (range 3-32 months); follow-up visits were usually necessary for neurological examination.

Table 1. Signs, symptoms, and associated injuries among 49 patients with brachial artery injury.

Presentation	No. of patients
Pulse deficit	43
Pulse insufficiency	6
Hemorrhage	34
Hypotension	20
Peripheral nerve injury	11
Venous injury	14
Tendinous injury	8
Hematoma	8
Bone fracture	5
Pseudoaneurysm	1
Ischemia	28

DISCUSSION

Penetrating trauma is generally considered to be the most common cause of a vascular injury in the upper extremity.[5] In addition to the usual types of blunt and penetrating injuries, supracondylar fractures or dislocation of the humerus may injure the brachial artery.[3]

The role of angiography in patients with brachial artery injury appears to be controversial.[9] Upper extremity arterial injury often can be managed without arteriography, particularly in cases with penetrating trauma[6] as seen in this series. Bynoe et al[7] has reported 99% sensitivity and 98% accuracy of duplex ultrasonography. Furthermore, duplex ultrasonography has no interventional risks and is more cost-effective for screening such injuries than angiography. Doppler ultrasonography was found to be more sensitive than angiography in an experimental trial, thereby supporting its use in the trauma setting.[8] Doppler ultrasonography of the upper extremity has been shown to be as specific and sensitive as arteriography in detecting brachial artery injuries.[9] If uncertainty remains regarding vascular injuries after physical examination and Doppler ultrasonography, angiography may be performed to confirm vascular injury.[9]

The mainstay of diagnosis of brachial artery injury in our study was based on clinical assessment and hand-held Doppler examination. Doppler ultrasonography was carried out in stable patients with associated soft signs of injury, to make a conclusive decision. We believe that angiography remains an effective method for diagnosing the vascular lesions, but it is also a time-consuming procedure, especially in traumatic vascular injuries

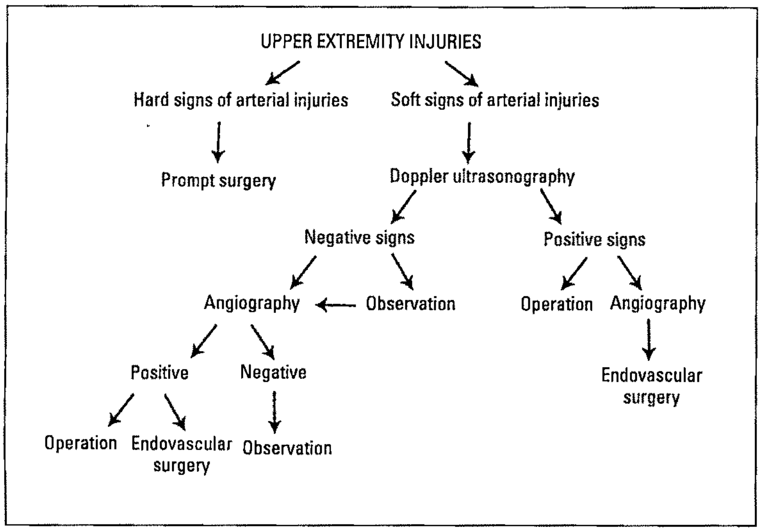

Figure 1. Diagnostic and therapeutic algorithm for upper extremity arterial injuries (soft signs include cool extremity, color change and nonexpanding hematoma).

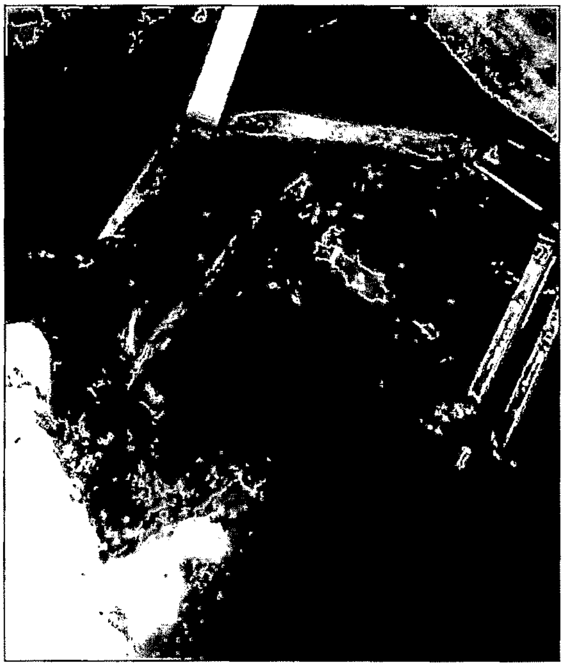

Figure 2. Reconstruction of crushed brachial artery with saphenous vein interposition graft.

requiring prompt surgery. Additionally, preoperative angiography did not offer any benefits in patients with obvious arterial injury. Angiography may be useful, especially in patients with multiple sites of potential vascular injury.[10] We have used angiography in patients with stable axillary artery injury associated with chest trauma causing subcutaneous emphysema, which prevented ultrasonographic examination. Additionally, angiography must be used during endovascular surgery.

Normally the average brachial-brachial Doppler pressure index between the 2 upper extremities is approximately 0.95; it is rarely less than 0.85.[11] In our serious, preoperative values were significantly lower than normal, but postoperative values were similar to normal. Duplex ultrasonography is fairly reliable, except with minor injuries, depending on the experience of the sonographers.[2] However, in addition to assessing the upper extremity for pulse pressures by physical examination and continuous-wave Doppler, neuromuscular function, soft tissue involvement, and skeletal integrity should be evaluated.[1]

The timing of vascular repair in relation to fracture management has long been a source of controversy. Because prevention of prolonged tissue ischemia is the objective, the standard recommendation is for vascular repair to precede fracture management.[12] In contrast, Hunt et al[13] suggested that arterial revascularization should be followed by skeletal stabilization and nerve and tendon repair. In the rare instance when external fixation is immediately required to stabilize the limb following massive musculoskeletal trauma, temporary selective use of shunts to restore circulation may be used to allow rapid fixator placement, with later vascular and orthopedic repair.[1] Unstable fractures jeopardize arterial repairs more in the upper extremities than in the lower extremities because of less adjacent muscle.[14] Therefore, we have routinely controlled the repaired vessels after bone fixation for patency.

Surgical repair of brachial artery injuries can be accomplished by a variety of techniques, including lateral repair, resection with end-to-end anastomosis, or interposition grafting, usually with a saphenous vein.[3] End-to-end anastomosis is preferable if it can be performed without tension or damage to major collateral vessels. Otherwise, the saphenous vein interposition graft is the next best choice, because it has better patency rates and better resistance to infection compared with synthetic grafts.[15] However, we had to use a ringed polytetrafluoroethylene (PTFE) graft in one patient with inadequate saphenous vein. Endovascular techniques have increasingly been used in the management of penetrating injuries and may have some advantages even in blunt trauma.[16] They are especially ideal for managing blunt axillary artery injuries that are anatomically difficult to repair.[1]

It is important to limit the period of ischemia, and so minimize the degree of ischemia-reperfusion injury and the systemic consequences after the arterial repair. The extent of ischemia-reperfusion injury is directly proportional to the severity and duration of striated muscle ischemia. Beyond a golden period of 6 to 8 hours of ischemia, ischemia-reperfusion injury will endanger the viability of the limb and sometimes even the patient's life.[2] In this series, while 9 patients experienced a duration of ischemia longer than this period, there was only one amputation. The infrequent need for amputation was probably related to the rich collateral circulation in the upper limb of most patients.[2,17] Therefore, we suggest that all patients without obvious necrotic changes should be operated on irrespective of time interval between the beginning of trauma and arrival to the operating room, as was done in this series.

Neurological injury continues to destroy the function of the upper extremity even after a successful arterial repair.[9] The rate of functional disability ranges from 27% to 44% when injury to the upper extremity includes nerve injuries.[18] Nichols and Lillehei[19] recommend primary nerve repair for penetrating trauma (lacerations and stab wounds), while with gunshot wounds, because of the degree of contusion, acute nerve repair is rarely indicated.[20] Additionally, major venous injuries, fractures and widespread tissue destruction may also influence the long term function of the extremity.[21]

Venous injuries generally remain unrecognized until surgical exposure. The indication for venous repair in the upper limb is not clear. Injuries of the brachial or arm veins can be treated by ligation, as edema is rare. However, in the case of a severe soft-tissue injury where maximal venous return is necessary, venous repair is probably warranted.[5] We would add that brachial venous continuity, when possible, is maintained.

In conclusion, the elbow, like the shoulder, is known to have extensive collateral circulation that may mask the signs of acute arterial injury,[22] but whether this circulation is adequate is debatable.[23] Therefore, all brachial artery injuries should be repaired. Careful clinical examination, Doppler ultrasonography and pressure measurements are as important as angiography in the diagnosis of vascular injuries.[9] Also, the superficial location of brachial artery makes the diagnosis relatively simple. Therefore, brachial artery injuries may be diagnosed without angiography. We believe that angiography should be performed when the vascular injuries would be impossible to diagnose with other diagnostic modalities or when endovascular procedures are required. Prompt and appropriate management of the brachial artery injuries, attention to associated injuries and a readiness to revise the vascular repair early in the event of failure will maximize patient survival and upper extremity salvage.

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original article

Extracorporeal circulatory systems in the interhospital transfer of critically ill patients: experience of a single institution

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Ann Saudi Med 2009; 29(2): 110-114

BACKGROUND AND OBJECTIVES: Critically ill patients with acute circulatory failure cannot be moved to other institutions unless stabilized by mechanical support systems. Extracorporeal heart and lung assist systems are increasingly used as a bridge to end-organ recovery or transplantation, and as an ultimate rescue tool in cardiopulmonary resuscitation.

PATIENTS AND METHODS: From July 2001 to April 2008, we had 38 requests for extracorporeal support for interhospital transfer carried out by the air medical service. Respiratory failure was present in 29 patients, who were provided with pumpless extracorporeal lung assist (PECLA) or veno-venous extracorporeal membrane oxygenation (ECMO). Cardiac failure dominated in 9 patients, who underwent implantation of extracorporeal life support (ECLS). Underlying diseases were acute respiratory distress syndrome in 15 patients, pneumonia in 7, prior lung transplant status in 4, cardiogenic shock in 7, and septic shock in 4.

RESULTS: All assist systems were connected via peripheral vessels by the Seldinger technique. Transport was uneventful in all cases with no technical failures. On arrival at the specialized care hospital, two patients had leg ischemia and underwent relocation of the arterial cannula. After a mean (SD) support of 5.1 (3.0) days for PECLA, 3.5 (2.9) days for ECLS, and 7.3 (5.8) days for ECMO, 60%, 66%, and 66% of patients, respectively, could be successfully weaned from the systems. Discharge rates were 45% for PECLA, 44% for ECLS, and 56% for ECMO.

CONCLUSION: Our experience proves that minimized extracorporeal assist devices allow safe assistance of patients with isolated or combined heart and lung failure in need of interhospital transfer. Critically ill patients get a chance to reach a center of maximum medical care.

Interhospital transfer of patients with acute cardiac failure (i.e., cardiogenic shock) to specialized medical centers is necessary for patient survival, especially in highly catecholamine-dependent and mechanically ventilated patients.[1] Patients with severe respiratory failure (acute respiratory distress syndrome) as a result of generalized disease or severe trauma, including military personnel, are another group of patients frequently requiring transport to specialized care institutions.[2-4] The use of extracorporeal perfusion systems during transportation minimizes risk and avoids cardiovascular instability.[5] There is little difference between transport within a clinical center or between locally separated institutions. The relevant logistic and security efforts are the same.[6] This report reviews the technique and equipment required for interhospital extracorporeally assisted transport and evaluates patient outcome in our experience.

PATIENTS AND METHODS

From July 2001 to April 2008, the Department of Cardiothoracic Surgery, University Hospital, Regensburg, Germany, had 38 requests for extracorporeal assistance in interhospital transfer missions carried out by the air medical service. The transport team included an anesthesiologist experienced in cardiopulmonary bypass, a perfusionist, a nurse or paramedic and a cardiac surgeon in cases of cardiogenic shock. Preparation time for the team was about 20 to 40 minutes after receiving a request. For air medical transfer, a rescue helicopter (Messerschmitt-Bölkow-Blohm BK-117) of the air rescue center in Regensburg was available. For ground transport, a special intensive care transport vehicle was used. After arrival of the transport team, a clinical assessment was performed to determine which assist device was most appropriate for the patient. The indication for extracorporeal lung- or heart- and lung-assistance is insufficient pulmonary gas exchange (hypoxemia/hypercapnia) during forced artificial ventilation. The appropriate system was assembled and primed, and the cannulas placed by the anesthesiologist and the perfusionist of the air medical service. Before initiation, 5000 units of heparin were given, except in patients with severe coagulopathy. Patient monitoring was the same as in the intensive care unit. Systemic anticoagulation was withheld for up to 24 hours after the start-up of extracorporeal assist as some patients had a high risk of bleeding (postoperative severe multiple trauma). Systemic anticoagulation was carried out via heparin perfusion pump. The effect of heparin was measured by the activated partial thromboplasin time. Patients without any particular risk of bleeding were given a dose of 50 mg to 100 mg acetylsalicylic acid (Apisol) every other day. In this case the aim was to assure the gas exchange capacity of the membrane oxygenator for the time of platelet aggregation inhibition.

In general, three systems are available for extracorporeal gas exchange. The underlying disease (isolated pulmonary failure or combined cardiopulmonary failure) defines the perfusion system required. The integral component of all systems is an extracorporeal module for gas exchange, i.e. an oxygenator. PECLA (pumpless extracorporeal lung assist) or interventional lung assist (iLA) is an extracorporeal gas exchange procedure designed by an interdisciplinary team at the Department of Cardiothoracic Surgery, University Hospital Regensburg in 1996.[7] This arterio-venous bypass procedure uses the patient's blood pressure (the mean arterial pressure) as the driving force for the blood flow through an oxygenator. Accordingly, only patients with an adequate blood pressure and sufficient cardiac output are suitable candidates for this procedure. PECLA is primarily indicated in patients with inadequate elimination of CO_2, such as in respiratory acidosis, as oxygen transfer is much less effective with this procedure.[8] PECLA was developed to support pulmonary function in patients with severe respiratory insufficiency. The best indication is severe hypercapnia and moderate hypoxia.[9] About 1-2 L/min are bypassed into the PECLA circuit. In our center, the PECLA membrane oxygenator (Novalung GmbH, 72379 Hechingen, Germany) is used on intensive care wards as well as for patient transport. The necessary priming volume is low (300 mL). Cannulas (NovaPort, Novalung, Hechingen, Germany) are placed via the Seldinger technique into the femoral artery (15-17 Fr) and femoral vein (17-19 Fr) (Figure 1). ECMO (extracorporeal membrane oxygenation) is a veno-venous extracorporeal bypass procedure used during severe global respiratory failure, such as acute respiratory distress syndrome, where cardiac pump function is not essentially affected. Via extracorporeal lung support sufficient gas exchange is created to treat critical hypoxemia and hypercapnia. The blood is drained from the inferior vena cava and diverted into the superior vena cava by a centrifugal pump (3-4 L/min). Lung protective ventilation may be added during extracorporeal gas exchange but is not essential. ECLS (extracorporeal life support) is a veno-arterial bypass procedure for emergency cardiopulmonary situations.

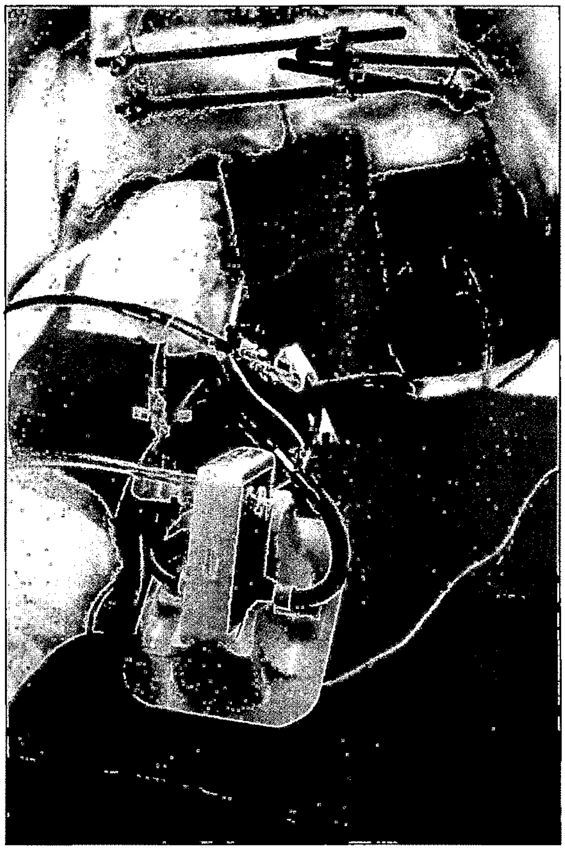

Figure 1. PECLA system with gas exchange membrane visible, along with ultrasound chip for measurement of blood flow.

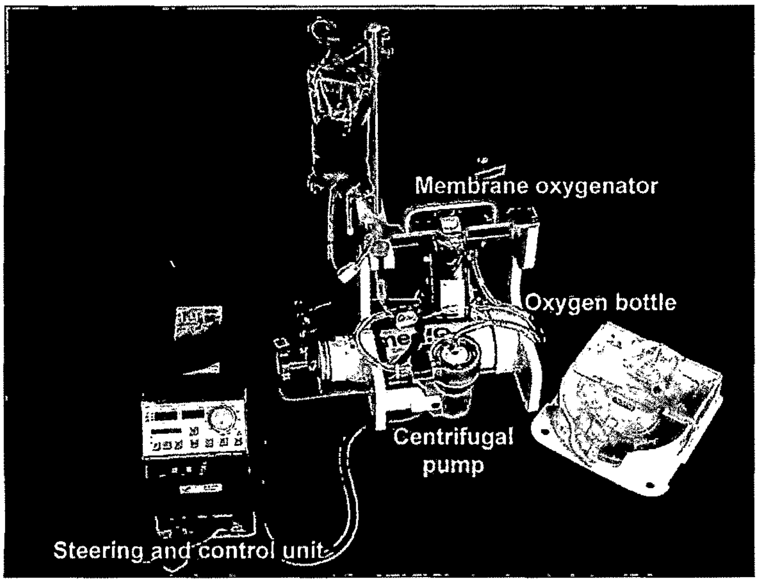

Figure 2. Emergency MECC system.

Table 1. Blood flow and cannulation site for different techniques.

	Blood flow
iLA/PECLA	Femoral artery to femoral vein
ECLS	Femoral vein to femoral artery
ECMO	Femoral vein to jugular vein

iLA: interventional lung assist, PECLA: pumpless extracorporeal lung assist, ECLS: extracorporeal life support, ECMO: extracorporeal membrane oxygenation.

The indication for use is acute circulatory failure with or without pulmonary malfunction. Patients may suffer from primary heart disease (e.g. acute myocardial infarction) or from an unsuccessful intervention (failed PTCA or CABG).

Transport of patients with severe cardiopulmonary failure is only possible with a mobile minimized extracorporeal support system (Figure 2). An emergency mobile minimized extracorporeal support system was developed in our institution, based on the MECC system from Maquet (Rotaflow, Maquet, Germany). It allows effective cardiorespiratory stabilization prior to and during transfer in an air or ground ambulance. The main components are a multifunctional holder with an oxygenator and a centrifugal pump, as well as a 2-liter oxygen bottle and a flow-regulator FM 41L 0-15 L/min (Dräger AG, Lübeck, Germany). The total weight of the equipped multifunctional holder is about 11 kg. The pump control is separate and provided with a carrying belt (16 kg). The complete system can be carried by one person, but can also be fastened on an ordinary stretcher of an ambulance vehicle. For combined life support and patient transport we use the "Emergency Life Support Set (ELS)" (Maquet Cardiopulmonary AG, 72145 Hirrlingen, Germany), which is heparin coated (Bioline Coating, Maquet Cardiopulmonary AG). The ELS set was modified as both Luer connectors were removed from the centrifugal pump after the priming (600 mL) to avoid air entrance in the negative pressure region of the extracorporeal circuit. All necessary components for percutaneous access (from covering cloths to cannula sets) were stored in a single box (60×40×35"). In patients with ECMO and ECLS systems, a 23 French femoral cannula (BFV 900-312, Sorin Group Munich, Germany) was used for venous drainage. In ECMO patients, the blood was returned via a cannula (15-17 Fr) into the internal jugular vein or the right subclavian vein. In patients with an ECLS, blood recirculation was into the common femoral artery. All cannulas were inserted percutaneously employing the Seldinger technique (Table 1).

RESULTS

A total of 38 patients in external hospitals were connected to the extracorporeal gas exchange systems prior to interhospital transfer (Table 2). Respiratory failure was present in 29 patients, who were provided with PECLA with or without ECMO (Table 3). Cardiac failure dominated in 9 cases, which underwent implantation of an ECLS. After local evaluation 20 patients were provided with PECLA systems, whereas 9 patients each were provided with ECLS and ECMO systems. Twenty-four of 38 patients were successfully weaned (63%) and 18 patients (47%) were discharged from the hospital (Table 4).

Patients in the PECLA group had a mean (SD) PaO_2/FiO_2 ratio of 55 (5) mm Hg and a mean (SD) $PaCO_2$ of 70 (10) mm Hg before device implantation. After referral to our institutions and further mechanical support with the PECLA system for 5.1 (3.0) days, 12 of 20 patients (60%) could be successfully weaned, while 8 patients (40%) died on the system. Finally, 9 of the 20 patients were discharged from the hospital without residual pulmonary impairment (45%).

Patients in the ECLS group were hemodynamically unstable and required a mean (SD) norepinephrine dosage of 7.6 (4.7) µg/kg/min to stabilize the circulation before placement of the veno-arterial bypass. Two hours after device insertion, the mean norepinephrine dosage could be reduced to 1.9 (1.1) µg/kg/min. During transport the pump flow was 3.0 (0.5) L/min. After continuous support for 3.5 (2.9) days, 6 of 9 patients were weaned. Four of 9 patients were discharged

Table 2. Demographic data on the 38 interhospital transfer patients.

System	n	Mean (SD) age (years)	Gender (male/female)	Mean (SD) transport distance (km)	Transport (helicopter/ITV)
iLA/PECLA	20	35.9 (14.5)	17/3	227 (161)	14/6
ECLS	9	51.1 (8.9)	8/1	77 (23)	7/2
ECMO	9	40.9 (19.5)	5/4	105 (59)	7/2

ITV: intensive care transport vehicle, iLA: interventional lung assist, PECLA: pumpless extracorporeal lung assist, ECLS: extracorporeal life support, ECMO: extracorporeal membrane oxygenation.

Table 3. Diagnoses and extracorporeal systems used in 38 interhospital transfer patients.

Diagnoses	iLA/ PECLA	ECLS	ECMO
ARDS post-trauma	8	-	3
ARDS	3	-	1
Pneumonia	7	-	1
Pre-lung transplantation	2	-	2
Cardiogenic shock	-	6	1
Septic shock	-	3	1
Total	**20**	**9**	**9**

ARDS: acute respiratory distress syndrome, iLA: interventional lung assist, PECLA: pumpless extracorporeal lung assist, ECLS: extracorporeal life support, ECMO: extracorporeal membrane oxygenation.

Table 4. Overall mechanical support and patient outcome.

Group	n	Support (days)	Weaning (n)	Discharged from hospital (n)
iLA/ PECLA	20	5.1 (3.0)	12	9
ECLS	9	3.5 (2.9)	6	4
ECMO	9	7.3 (5.8)	6	5

iLA: interventional lung assist, PECLA: pumpless extracorporeal lung assist, ECLS: extracorporeal life support, ECMO: extracorporeal membrane oxygenation.

from the hospital (44%).

The two patients in the ECMO group had terminal lung failure. Accordingly, the intention of the device implantation was not only a safe transport to a primary care institution, but also a consecutive bridging to lung transplant, which was successful in both patients. Of the 7 remaining patients, 4 were weaned from the system after a total support of 7.3 (5.8) days, while 3 patients died during support. Eventually, 5 of the 9 patients were discharged from the hospital (56%).

During transport no malfunctions of the extracorporeal perfusion systems occurred, even though the mechanical demands (vibration) were considerable (e.g. during start and landing with a helicopter). During an interhospital transfer over the distance of 350 km an acute stop over became necessary on one occasion when the oxygen supply was insufficient. In another case, the gas exchange module of a PECLA system had to be exchanged after the recoiling hose assembly to the femoral vein had buckled for a short while and a partial thrombosis of the membrane oxygenator ensued. During in-hospital treatment, 2 patients with femoro-femoral ECLS developed compartment syndrome in the respective lower extremity, which necessitated a relocation of the femoral artery cannula to the right subclavian artery. Another patient developed heparin-induced thrombocytopenia type II with thrombosis of the pump head on the sixth day of support. The pump head was changed and the anticoagulation changed to argatroban (Argatra, Mitsubishi Pharma Europe Ltd, London). The gas exchange capacity of the oxygenator was not affected so it was not necessary to exchange the oxygenator.

DISCUSSION

The interhospital transfer of patients with the aid of extracorporeal perfusion systems is not a new procedure.[10-12] Foley and Bartlett had reported on more than 100 patients by 2002.[13] However, considerable logistical, technical and human effort is required. The perfect operation of the extracorporeal circulation equipment without complications is important to successful interhospital transfer. Foley noted a complication rate of 17% associated with the system. Our approach in the development of transportable extracorporeal circulation systems was make the device as simple as possible including one module for gas exchange and one blood pump only. A new portable transport device for ECLS and ECMO was based on the MECC system of the

Maquet company, which had been developed and routinely applied in our hospital in more than 1600 aortocoronary bypass operations.[14] The PECLA system was identical to that used in the intensive care setting.

Air medical services using extracorporeal assistance pose a special challenge. The gas exchange capacity in the oxygenator decreases with the lowering of atmospheric pressure; in other words, if an oxygenator is used at high altitude, there is a reduced O_2 transfer rate. Our flight altitude was always below 5000 feet (1524 meters). As a result, the reduced atmospheric pressure had only a minimal effect on O_2 transfer, with a mild desaturation of 3% to 4%. During a flight at 2300 meters (6900 feet), the oxygenator ventilated with an FIO_2 of 1.0 would have the same capacity as at sea level with an FIO_2 of 0.8. Forces of acceleration and forces of deceleration may affect the patient as well as the extracorporeal perfusion system during air transport, but we observed no blood volume shifting in the patient or perfusion system. We also had no problems with the venous return during take-off and landing, which may have been due to the use of helicopters instead of airplanes as helicopters mostly remain in a horizontal position.

Apart from the technical equipment, the qualifications and experience of the transport team plays a crucial role in the success of interhospital transfer. Experience in severe critical care patient management and percutaneous application of the cannulas is necessary as well as safe handling of the miniaturized perfusion system. In hospitals without vascular surgical stand-by, percutaneous arterial cannula placement carries considerable risk since small vessels may require surgical revision and anastomosis of a Dacron prothesis for cannula insertion. The placement of venous cannulas is less prone to complications.

In conclusion, our experience proves that miniaturized extracorporeal assist devices allow for the safe transport of critically ill patients with isolated or combined heart and lung failure.

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original article

Paraumbilical hernia repair during cesarean delivery

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Ann Saudi Med 2009; 29(2): 115-118

BACKGROUND AND OBJECTIVES: Pregnant women with paraumbilical hernia usually postpone hernia repair until after delivery, but some patients request that it be done during cesarean delivery. Therefore, we evaluated the outcome of combined cesarean delivery and paraumbilical hernia repair in a prospective study at a tertiary referral university hospital.

PATIENTS AND METHODS: In a prospective study, we compared the outcome of 48 patients undergoing cesarean delivery combined with paraumbilical hernia repair versus 100 low-risk patients undergoing cesarean delivery alone. The main outcome measures were operation time, blood loss, severity of pain, peripartum complications, hospital stay, hernia recurrence, and patient satisfaction.

RESULTS: The combined procedure took significantly longer than cesarean delivery alone (75.2 minutes versus 60.5 minutes, P<.001)). There were no major complications. Wound infection occurred in 6 patients (4.1%). Hospital stay did not differ significantly from those of controls. Pain at the hernia site repair occurred in two patients, and one hernia recurred in the hernia repair group during a mean follow-up period of 22 months (range, 6-36 months). All hernia patients reported that they preferred the combined operation.

CONCLUSIONS: Combined cesarean delivery and paraumbilical hernia repair had the advantage of a single incision, single anesthesia, and a single hospital stay while avoiding re-hospitalization for a separate hernia repair. Our results indicate that the combination approach is safe, effective, and well accepted.

Umbilical hernias account for 6% of all abdominal wall hernias in adults.[1] There is no consensus on the best technique for the repair of umbilical hernia and thus various surgical techniques such as primary suture, Mayo repair, mesh repair, and laparoscopic surgery have been used for the treatment of this surgical condition.[2] Cesarean delivery has been practiced over the centuries, but only relatively recently has it became such a safe procedure that women are requesting that it be used to deliver their baby in the absence of any other indication.[3] The combination of umbilical hernia repair with gynecologic surgery or cesarean delivery is virtually undocumented except for a case report from 1987[4] and another report of 8 patients having inguinal and umbilical hernia repaired during cesarean delivery.[5] However, the combination of paraumbilical hernia repair with abdominal surgery remains unstudied except in conjunction with cholecystectomy.[6,7] The practice is uncommon, probably because most obstetricians believe that any additional risk from combined surgery is unwarranted since repair of paraumbilical hernia is rarely urgent. We have offered a hernia repair in conjunction with cesarean delivery since 2004 to patients with a paraumbilical hernia during pregnancy (if a cesarean delivery were planned). The aim of this study was to compare the outcome in this group with that of a low-risk control group undergoing cesarean delivery alone at the same institution.

PATIENTS AND METHODS

In a prospective study, we compared the outcome of 48 pregnant women who underwent a paraumbilical hernia repair in combination with a scheduled elective cesarean delivery between January 2004 to January 2006 with that of a control group of 100 pregnant women who underwent caesarean delivery alone during the same period. Outcome measures assessed included operative time, postoperative complications, and length of

Table 1. Age, parity and gravidity in the study population (group I: combined hernia and cesarean delivery; group II: cesarean delivery alone).

	Group I (n=48)	Group II (n=100)	F ratio	*P* value
Age (y)	30.6±2.6	28.6± 2.6	1.057	.8
Parity	2.1±1.1	1.5±1.0	1.125	.61
Gravidity	3.4±1.1	2.7±1.0	1.159	.53

Values are mean±SD. CD: cesarean delivery

Table 2. Indications for cesarean delivery, operative time, hospitalization time and pre- and postoperative mean hemoglobin in the study population (group I: combined hernia and cesarean delivery; group II: cesarean delivery alone).

	Group I (n=48)	Group II (n=100)	*P* value
Indications for CD			
Primary cesarean delivery			
CPD	1 (2.8%)	2 (2.0%)	.7
Failure to progress	9 (18.8%)	18 (18.0%)	.9
Malpresentation	4 (8.3%)	9 (9.0%)	.8
PROM	3 (6.3%)	7 (7.0%)	.8
Repeat cesarean delivery	31 (64.6%)	64 (64.0%)	.9
Operative time (minutes)	78.2±19 (55-120)	60.4±10 (45-90)	<.001
Hospital stay (days)	3.6±0.86	3.4±1.2	.21
Preoperative hemoglobin (g)	12.5±5.7	13.4±6.2	.35
Postoperative hemoglobin (g)	11.4±4.5	12.2±5.3	.38

Values are mean (SD) or number of patients and percentage. CPD: cephalopelvic disproportion; PROM: premature rupture of membranes

Table 3. Postoperative analgesic use and complications (group I: combined hernia and cesarean delivery; group II: cesarean delivery alone).

	Group I (n=48)	Group II (n=100)	*P* value
Analgesic ampule use (mean per week)	4.97 (1.2%)	4.59 (0.9%)	.027
Wound sepsis	2 (4.2%)	4 (4.0%)	.26
Seroma	1 (2.1%)	2 (2.0%)	.31
Wound disruption	0 (0.0%)	1 (1.0%)	.17

Values are mean (SD) or number of patients and percentage.

hospital stay. The control group were free of medical problems as diabetes, heart disease, and anemia or other conditions that might place them at greater risk of complications. The 48 women provided informed consent to undergo cesarean delivery combined with primary hernia repair. Cesarean delivery was conducted as follows: the skin was disinfected with bovidine iodine; a Pfannenstiel skin incision was made in the lower crease; the fetus was delivered; the uterine wound was closed, all the while maintaining good hemostasis. All patients received antibiotic prophylaxis in the form of intravenous cefotaxime sodium 1 gram after placental extraction. In 36 patients who had a defect less than 3 centimeters we performed umbilical hernia repair by means of a primary suture from the inside. In 12 patients with a defect more than 3 centimeters, repair was performed by inside mesh hernioplasty fixed to the peritoneum and sheath by non-absorpable polypropylene suture. Good peritoneal toilet and closure of the cesarean wound was done as usual. Postoperative pain was evaluated by the average consumption of analgesic ampules given on patient demand during the first week. All patients received a routine intramuscular dose of 75-mg dose of diclophenac sodium (Voltaren IM; Novartis, Basel, Switzerland) twice on the day of the operation. The same analgesic was given as needed later. Total analgesic consumption was recorded during the first postoperative week. Wound infections, separations, seromas and hematomas were treated with local care and/or antibiotics, on an outpatient or in-patient basis as the situation required. Wound infection was diagnosed if the wound drained purulent material or the incision required opening and showed two or more of the classical signs of infection, such as erythema, tenderness, induration, and fever. Wound seroma or hematoma was diagnosed in the presence of a serous fluid collection or subcutaneous blood without signs of infection. Wound disruption was defined as spontaneous or iatrogenic separation of the wound edges more than 1 cm. The patients were followed-up postoperatively daily until discharge from the hospital, then every 3 days as an outpatient for the first 2 weeks, then 1 month later, and finally every 6 month. Descriptive statistics are shown as the mean±standard deviation. Statistical analyses were done with the t test, Mann-Whitney U test, and Kruskal-Wallis test as appropriate.

RESULTS

There were no significant differences in age, parity or gravidity between the patients that had cesarean delivery plus hernia repair (group I) and those who had cesarean delivery alone (group II) (Table 1). Repeated cesarean delivery was the most common indication for cesarean delivery in both groups (other indications are listed in Table 2). Mean operative time was significantly longer (P<.001) in group I compared with group II, but the mean length of hospital stay was similar in the two groups (P=.21) (Table 2). No significant difference was found between pre- and postoperative mean hemoglobin levels (Table 3). The patients in group I reported more pain; the need for analgesics was significantly less in group II (P=.027). The rate of early and late postoperative complications such as seroma and/or hematoma, wound infection, and wound disruption was similar in the two groups (Table 3). There was one recurrence (2.8%) in the suture repair subgroup, whereas no recurrence was detected in the mesh hernioplasty subgroup. The mean follow-up time was 22 months (range, 6 to 36 months). Caesarean delivery suture healing was delayed, with wound infection in 6 patients (2 in group I and 4 in group II). The patients expressed subjective satisfaction and preferred the combined procedure. No postoperative mortality was observed. The recurrence rate in patients in the suture-receiving subgroup was statistically significant when compared with patients in the mesh-receiving subgroup (P<.03).

DISCUSSION

Paraumbilical hernias are prone to incarceration and continue to enlarge if untreated, and thus they should be considered for repair at presentation.[8] Our analysis of the potential benefit of combining cesarean delivery with hernia repair resulted in no increase in complications (notably infection) over cesarean delivery alone. Furthermore, all patients continued to be satisfied with the combined procedure up to 3 years later. The practical benefits were obvious: a 2-in-1 operation, with a single incision, single anesthesia, and single hospital stay, conferring valuable advantages for both patient and hospital in time, cost, and convenience, not to mention avoiding the separation of mother from newborn entailed by re-operation. In our opinion, the intraoperative difficulty of mesh fixation and to a lesser extent primary suture repair is the main problem, which always requires assistance to achieve good traction. Proponents of postpartum hernia repair may argue that the combined procedure increases the complication rate, because of blood loss and wound infection resulting from the longer operation time, and prolongs hospitalization. Our data refute this view. Hernia repair prolonged the average duration of cesarean delivery, but the time remained within the normal range reported for hernia repair in the literature.[9] In all patients undergoing paraumbilical hernia repair, operation times remained below 120 minutes with a wound infection rate in our series of 4.2%, a little lower than the reported 6.2% within this time limit.[9] Wound healing was delayed, with infection, in 6 patients. Hospitalization was not prolonged in patients undergoing the combined procedure. Disruption of the abdominal incision is a major source of morbidity after cesarean delivery. Failure of the abdominal skin incision to heal commonly occurs because of infection, abscess, hematoma, and seroma formation. Postoperative abdominal wound infection is a common cause of morbidity and has been reported to occur in 5% of patients.[10,11] In our series seroma formation occurred in 3 patients (2%) and wound disruption occurred in 1 patient (0.68%). Forty-eight cases may appear few, but to our knowledge there is no equivalent series in the literature except for a series of 8 patients with inguinal as will as umbilical hernias.[5] In these 8 cases, only 3 had umbilical hernia repaired during cesarean delivery and complication and recurrence rates were zero. Despite the high frequency of the umbilical hernia repair procedures, disappointingly high recurrence rates, up to 54% for simple suture repair, are reported.[12] Large differences in hernia recurrence rates have been reported: between 10% to 30%, depending on surgical technique, length of follow-up, and method of recurrence assessment.[12] Rates also increase with time, with most recurrences occurring early, in the first 3 months after mesh repair.[13-14] In our study, the recurrence rate was 2.8% for the suture repair group and there was no recurrence in the mesh group, which is low if compared with the above reported rates.

Whether it is best to repair a pregnancy hernia during the pregnancy itself, at cesarean delivery or postpartum after involution of the uterus, remains a matter of dispute. Some authors recommend repair during pregnancy only in the case of strangulation and incarceration. Some have recommended repair of irreducible umbilical hernias before the enlarging uterus caused possible strangulation.[15] Otherwise, if there are no complications during pregnancy, repair can be deferred until as soon as possible postpartum. One reason for deferral is that anesthesia and surgery during pregnancy could precipitate uterine irritability and induce premature labor, up to one week postoperatively.[15] Other proposed reasons have been the extreme vascularization of the uterus, and the induction of collagen remodeling by relaxin during pregnancy, with the softened tissue predisposing to hernia recurrence.[16]

In conclusion, cesarean delivery combined with paraumbilical hernia repair avoids rehospitalization and appears safe, effective, and well accepted. It neither increased the complication rate nor prolonged the hospital stay, and in our sample, it was associated with acceptable long-term recurrence (only one case). Confirmation of these results in a larger study, including other types of ventral hernia, would establish combined cesarean delivery and hernia repair as a recommendable procedure.

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original article

Optimal dosing of angiotensin-converting enzyme inhibitors in patients with chronic heart failure: a cross-sectional study in Palestine

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Ann Saudi Med 2009; 29(2): 119-122

BACKGROUND AND OBJECTIVE: Because high-dose angiotensin-converting enzyme (ACE) inhibitor therapy is desirable in patients with chronic heart failure (CHF), we sought to determine the usage and dosing patterns of ACE inhibitors in CHF patients at a governmental hospital in Palestine.
METHODS: This cross-sectional study was conducted between September 2006 and August 2007. All patients admitted with a confirmed diagnosis of CHF and an ejection fraction <40% were evaluated. After excluding patients with a caution/contraindication to ACE inhibitor use or not taking an ACE inhibitor, we determined the number of patients receiving optimal (captopril 150-300 mg/day, enalapril 20-40 mg/day, ramipril 5-10 mg/day) and suboptimal doses. We then conducted statistical analyses to evaluate associations between ACE inhibitor use and dosing and various demographic and clinical factors.
RESULTS: Of the 165 patients initially evaluated, 69 (41.8%) had a caution/contraindication (n=28, 40.6%) or were not using an ACE inhibitor (n=41, 59.4%). Of the remaining 96 patients (70.1%), 49/96 (51%) were given an optimal dose while 47/96 (49%) were given a suboptimal dose. Of all patients with CHF and no contraindication (n=137), 88 (64.2%) were either receiving no ACE inhibitor or a suboptimal dose. Only the presence of hypertension was significantly associated with the use of an ACE inhibitor (*P*=.009, odds ratio=2.7). The use of an optimal dose was not significantly associated with any of the tested factors (age, gender, presence of hypertension, diabetes mellitus, renal dysfunction, ischemic heart disease or number of diagnosis) .
CONCLUSION: Underutilization and suboptimal dosing of ACE inhibitors was common. Since there is an abundance of evidence in favor of using high-dose ACE inhibitor therapy in patients with CHF, physicians need to be educated about proper dosing of these agents.

Chronic heart failure (CHF) is an increasingly common clinical condition with high morbidity and mortality.[1] Current guidelines recommend that angiotensin-converting enzyme (ACE) inhibitors be used as first-line therapy for patients with CHF unless contraindicated.[2] The doses given to patients with CHF should be those proven effective in randomized clinical trials.[3-6] One study suggested that patients with CHF should be titrated to higher doses of ACE inhibitor therapy when possible.[7] Another study also found that clinicians should attempt to reach high doses in patients with CHF.[8] Even though low doses of ACE inhibitors have not been proven effective in reducing mortality,[9] low doses are superior to no therapy.[7] In light of this, we conducted this study to evaluate dosing with ACE inhibitors among patients with CHF at Al-Watani Hospital, a governmental hospital in Nablus, Palestine.

METHODS

This cross-sectional study was conducted at the Al-Watani Hospital between September 2006 and August 2007. All patients admitted to the hospital during this period with a confirmed diagnosis of CHF and a maximum ejection fraction value (EF) of 40%, indicative of systolic heart failure, were initially evaluated for inclusion in the study. All information on the clinical condition of the patient and medication for CHF were obtained from the medical files and from the patient directly by a clinical pharmacist in the hospital. The study was approved by the hospital administration.

We excluded patients with cautions/precautions and contraindications to the use of ACE inhibitors, which include the following: pregnancy, history of angioedema, hypersensitivity to the drug, cough, hepatic dysfunction, hyperkalemia (> 5.5 mEq/mL), hypotension, renal insufficiency (creatinine clearance <30 mL/ min), and aortic or renal stenosis.[10] For patients included in the study, the current type and dose of ACE inhibitor were determined. The use of an ACE inhibitor was defined as the current active use of the drug. The optimal dose was defined as any dose equal to or above the dose reported in the clinical trials that assessed mortality.[3-6] For captopril, the optimal dose was considered any dose ≥150 mg daily; for enalapril, it was ≥20 mg daily, and for ramipril, it was ≥5 mg daily.[3-6] Lower doses were considered suboptimal. If the patient was taking a suboptimal dose, but had recently been using the ACE inhibitor and was in the process of upward titration of the dose, he/she was considered to be taking an optimal dose.

Statistical analysis was carried out using statistical package for social sciences version 15. The chi-square test was used to test for significant associations between ACE inhibitor use and various categorical clinical and demographic factors as well as for association with optimal dosing. Results with $P<.05$ were considered statistically significant. The relative likelihood for the use of ACE inhibitor was estimated using an odds ratio (OR) calculated by means of cross tabulation analysis and provided with 95% confidence intervals (95% CI) for the odds ratios.

RESULTS

During the study period, 165 patients with CHF and an EF <40%, indicative of systolic heart failure, were interviewed and their medical [illegible] were reviewed. Twenty-eight patients (17%) had cautions/contraindications to the use of ACE inhibitors and were excluded from the analysis. Reasons for exclusions included intolerance or allergy to ACE inhibitors (n=3; 10.7%), renal insufficiency (n=21; 75%), and hyperkalemia (n=4; 14.3%). One hundred thirty-seven patients (83%) met the inclusion criteria. The average age (standard deviation) of this study population was 68.6 (10.4) years and 73 (53.3%) were females. Of the patients included, 95 (69.3%) had hypertension, 72 (52.5%) had diabetes mellitus, and 39 (28.4%) had a creatinine clearance <60 mL/ minute (Table 1).

Of the patients included in the analysis, 96 (70.1%) were using an ACE inhibitor while 41 (29.9%) were not (Figure 1). The use of an ACE inhibitor was significantly associated with hypertension, but not with sex, age, diabetes, ischemic heart disease, or renal function.

Table 1. Characteristics of 137 chronic heart failure patients based on the use of an ACE inhibitor.

Factor		Number of patients using ACE inhibitor (n=96)	Number of patients not using ACE inhibitor (n=41)	Odds ratio vs. other category (95% confidence intervals for use of ACE inhibitor)	*P* value
Sex	Male	45 (46.9%)	19 (46.3%)	1.02 (0.5-2.1)	.95
	Female*	51 (53.1%)	22 (53.7%)		
Hypertension	Yes	73 (76%)	22 (53.7%)	2.7 (1.3-5.9)	.009
	No*	23 (24%)	19 (46.3%)		
Ischemic heart disease	Yes	34 (35.4%)	12 (29.3%)	1.3 (0.6-2.9)	.50
	No*	62 (64.6%)	29 (70.7%)		
Diabetes mellitus	Yes	55 (57.3%)	17 (41.5%)	1.9 (0.9-3.9)	.09
	No*	41 (42.7%)	24 (58.5%)		
CrCl (mL/min)	≥60	68 (70.8%)	30 (73.2%)	0.9 (0.4-2.1)	.78
	<60*	28 (29.2%)	11 (26.8%)		
Age (years)	< 65	35 (36.5%)	12 (29.3%)	1.4 (0.6-3)	.42
	≥ 65*	61 (63.5%)	29 (70.7%)		

CrCl: creatinine clearance. *Reference category.

However, diabetic patients and patients younger than 65 years old were more likely to use an ACE inhibitor (Table 1). The types of ACE inhibitors and dosing information are shown in Table 2.

Of the patients using an ACE inhibitor, 49/96 (51%) were taking optimal doses while 47/96 (49%) were taking a suboptimal dose. Those taking suboptimal maintenance doses had no identifiable contraindication to the optimal dose. A total of 88/137 (64.2%) patients with CHF were either not taking an ACE inhibitor or were using a suboptimal dose in the absence of a contraindication to increase the dose to the optimal dose. Of the two most commonly used ACE inhibitors, dosage was significantly more optimal with enalapril compared to captopril (57.1% versus 30.4%; P=.026).

Statistical analysis indicated that none of the tested factors (age, gender, presence of hypertension, diabetes mellitus, renal dysfunction, ischemic heart disease or number of diagnosis) were significantly associated with use of an optimal dose of an ACE inhibitor, and thus no valid model could be built to predict the use of an optimal dose. However, patients <65 years of age (odds ratio=2.3, 95% CI 1 - 5.4), or patients with creatinine clearance >60 mL/min (odds ratio=2.0, 95% CI 0.8-4.8), or diabetic patients (odds ratio=1.8, 95% CI 0.8-4) were more likely to be using optimal doses.

DISCUSSION

Chronic heart failure is one of the major causes of mortality worldwide. Furthermore, the economic consequences of its management constitute a true burden on the health system,[11] which is why optimization of CHF therapy is of great importance. During the past 20 years, the many trials conducted in patients with CHF have concluded that ACE inhibitor use confers a 16% to 20% reduction in mortality.[12]

Underutilization or use of a suboptimal dose of an ACE inhibitor in patients with CHF seems common.[13] Variables that could affect the use of optimal doses of an ACE inhibitor include both physician and patient-dependent factors. One study found that regardless of physician specialty, approximately one-third of ACE inhibitor prescriptions are for suboptimal doses. Interestingly, the study also showed that general practitioners tend to prescribe higher doses than specialists.[14] Another study, which examined dosing and compliance with ACE inhibitors, concluded that efforts aimed at enhancing patient compliance and prescribing adequate dosages are needed.[15] Another study that quantified the extent and determinants of underutilization of ACE inhibitors for patients with CHF found that family practitioners and general internists probably underutilize ACE inhibitors

Table 2. Summary of the types and doses of ACE inhibitors used in patients with CHF.

	Captopril	Enalapril	Ramipril
Patients, n (%)	23 (17%)	70 (51%)	3 (2%)
Patients taking optimal dose, n (%)	7 (30%)	40 (57%)	2 (67%)
Patients on sub-optimal dose, n (%)	16 (70%)	30 (43%)	1 (33%)
Optimal dose (range in mg)	150-300	20-40	5-10
Mean (SD) daily dose (mg/d)	34 (15.5)	15.5 (11.9)	2.9 (1.9)
Median dose received (mg)	25	10	2.5
Minimum dose used (mg/d)	12.5	5	1.25
Maximum dose used (mg/d)	75	50	5

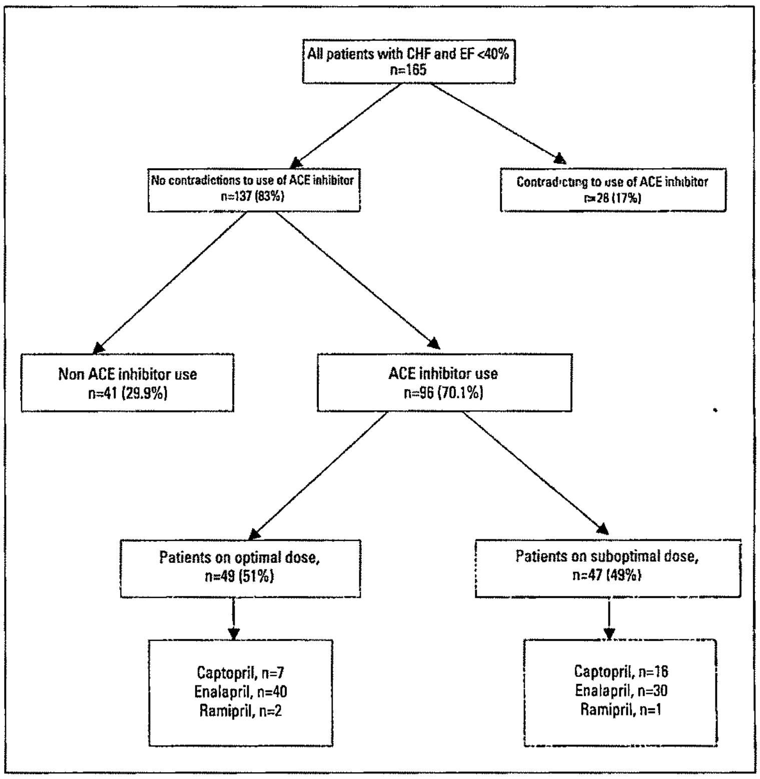

Figure 1. Overview of study results.

more often compared with cardiologists.[16] In the current study, the lack of association between ACE inhibitor use and most of the tested factors might suggest that ACE inhibitor use is determined by individual factors and that there is no particular pattern of use.

In our study, dosing was more optimal for patients who took enalapril. One possible explanation for more suboptimal dosing with captopril is that patients using that agent need to take three tablets daily to achieve the optimal target range because the highest available strength of captopril is 50 mg. In contrast, patients using enalapril need to receive only once or twice daily dosing of 10 mg or 20 mg of enalapril to reach the optimal target range.

Our study had some limitations. First, it is possible that the percentages of patients using optimal doses were underestimated. For example, some patients may have tried higher doses in the past, but had to discontinue because of an inability to tolerate the higher dose. Second, patients enrolled in the study are those who have governmental medical insurance. Therefore, the finding in this study could not be extrapolated to clinical practice in private clinics. To improve the dosing of ACE inhibitors in patients with CHF, continuing medical education for physicians is highly recommended. Furthermore, clinical pharmacists are needed to review medications and give advice to practitioners in hospitals.

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Tissue Microarray: A rapidly evolving diagnostic and research tool

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Accepted for publication November 2008

Ann Saudi Med 2009; 29(2): 123-127

Tissue microarray is a recent innovation in the field of pathology. A microarray contains many small representative tissue samples from hundreds of different cases assembled on a single histologic slide, and therefore allows high throughput analysis of multiple specimens at the same time. Tissue microarrays are paraffin blocks produced by extracting cylindrical tissue cores from different paraffin donor blocks and re-embedding these into a single recipient (microarray) block at defined array coordinates. Using this technique, up to 1000 or more tissue samples can be arrayed into a single paraffin block. It can permit simultaneous analysis of molecular targets at the DNA, mRNA, and protein levels under identical, standardized conditions on a single glass slide, and also provide maximal preservation and use of limited and irreplaceable archival tissue samples. This versatile technique, in which data analysis is automated, facilitates retrospective and prospective human tissue studies. It is a practical and effective tool for high-throughput molecular analysis of tissues that is helping to identify new diagnostic and prognostic markers and targets in human cancers, and has a range of potential applications in basic research, prognostic oncology and drug discovery. This article summarizes the technical aspects of tissue microarray construction and sectioning, advantages, application, and limitations.

Recent advances in the field of human molecular genetics have revealed gene-based disease mechanisms in many areas of medicine. The study of new prognostic and diagnostic markers in large numbers of clinical specimens is an important step in translating the new findings from basic science to clinical practice.[1] The investigation of the pathogenesis and progression of diseases such as cancer has been revolutionized with the increased use of new molecular biology techniques.[2] Elucidating the fundamental molecular mechanisms that are involved in the stepwise progression from normal tissues to malignant tumors is essential in our knowledge of cancers, and should ultimately lead to improved methods of detection, treatment, and cures for cancers.[3] Studies on clinical tissue have identified multiple novel markers, primarily at the gene level.[4] The validation of these markers using the standard histopathological techniques is time consuming, and labor intensive and costly, particularly when multiple markers are tested on numerous specimens.[4]

Tissue microarray is a recent innovation in the field of pathology that is expected to overcome these significant problems. The method was designed as a high-throughput molecular biology technique for researchers that allows for assessment of expression of interesting candidate disease-related genes or gene products simultaneously on hundreds of tissue samples.[5] It also allows parallel molecular profiling of clinical samples at the DNA, RNA, and protein level. This technique enables pathologists to perform large-scale analyses using immunohistochemistry, fluorescence in situ hybridization (FISH), or RNA in situ hybridization (ISH) at substantially faster and at markedly lower costs compared with conventional approaches.[1,6] This technology should not be confused with DNA microarrays where each tiny spot represents a unique cloned cDNA or oligonucleotide. In tissue microarrays, the spots are larger and contain small histologic sections from unique tissues or tumors.

This article provides a short review of this increasingly popular technology, focusing on several technical aspects of tissue microarray construction.This technology is relatively new and its use in developing countries has never been limited.[7-9] The technique was first reported 20 years ago by Battifora who described a "sausage block" method in which he wrapped 1 mm thick 'rods' of different tissues in a sheet of small intestine which was then embedded in a paraffin block and from which numerous sections were cut and examined.[10] The array format was first conceived by Wan and colleagues in 1987.[11] Although this technique conferred the significant advantage of simultaneously examining multiple tissue specimens under identical conditions, the inability to satisfactorily identify individual 'rods' limited any meaningful interpretation. These limitations were addressed subsequently, and in 1998, Kononen et al invented a device for rapid and accurate construction of tissue microarrays in a manner that is easily accessible to most pathology labs. The invention of this device and its commercialization led to a dramatic increase in the popularity and utility of the technique.[12]

Tissue microarray technique

Microarray is a technique for organizing minute amounts of biological samples on a solid support.[13] Tissue microarrays are composite paraffin blocks constructed by extracting cylindrical tissue core "biopsies" from different paraffin donor blocks and re-embedding these into a single recipient (microarray) block at defined array coordinates.[14,15] At first, the donor blocks (invariably stored paraffin blocks) are retrieved and sectioned to produce standard microscopic slides that are stained with hematoxylin and eosin. An experienced pathologist examines the slides to mark the area of interest, which is commonly an area of cancer (Figure 1), after which the samples can be arrayed.[4]

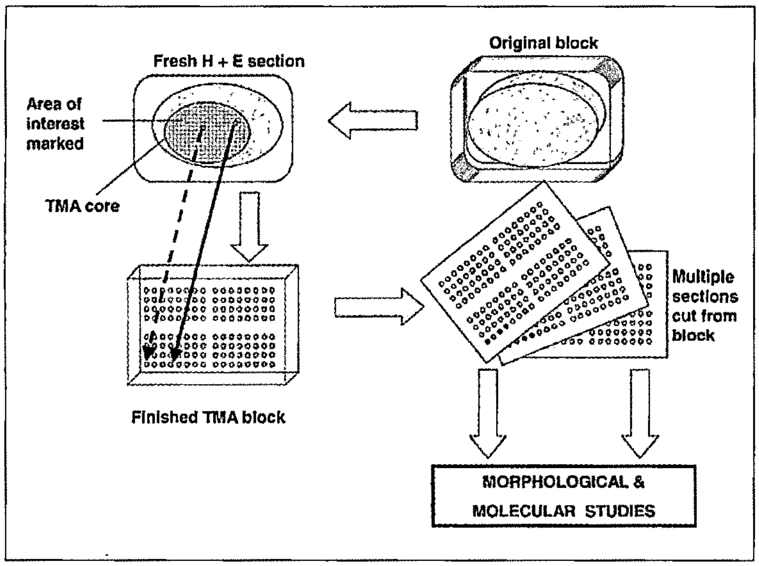

Figure 1. Construction of a tissue microarray (TMA).

A tissue microarray instrument (for example, Beecher Instruments, Winsconsin, USA, *www.beecher-instruments.com*) is used to acquire a tissue core from the donor block.[16] This core is then placed in an empty paraffin block—the recipient block (Figure 2).[16] The current Beecher Instruments arraying device is designed to produce sample circular spots that are 0.6 mm in diameter at a spacing of 0.7-0.8 mm.[17] The surface area of each sample is 0.282 mm^2, or in pathologists' terms, about the size of 2-3 high power fields. The number of spots on a single slide is variable depending on the array design; the current comfortable maximum with the 0.6 mm needle is about 600 spots per standard glass microscope slide.[15] The core is placed at a specifically assigned coordinate (X-Y guide), which is accurately recorded, typically on a spreadsheet, such as Microsoft Excel.[4] The sampling process can then be repeated many times from different donor blocks until hundreds, or even thousands, of cores are placed into one recipient block, producing the final tissue microarray block (Figure 2). Using a microtome, 5 μm sections are cut from the tissue microarray blocks to generate tissue microarray slides for molecular and immunohistochemical analyses (Figure 3).[16]

New technologies are under development that may allow as many as 2000 or more sections per slide. Using this method, an entire cohort of cases can be analyzed by staining just one or two master array slides, instead of staining hundreds of conventional slides.[18] Yet each spot on the array is similar to a conventional slide in that complete demographic and outcome information is maintained for each case so that rigorous statistical analysis can be done as rapidly as the arrays are analyzed.[15]

Advantages and applications of tissue microarrays

There are numerous advantages of tissue microarray over standard techniques, including:

Amplification of a scarce resource. A standard histologic section is about 3-5 mm thick, with variation depending on the submitting pathologist or technician. After use for primary diagnosis, the sections can be cut 50-100 times depending on the care and skill of the sectioning technician. Thus, on average, each archived block might yield material for a maximum of 100 assays.[13] If this same block is processed for optimal microarray construction it could routinely be needle biopsied 200-300 times or more depending on the size of the tumor in the original block. Once tissue microarrays are constructed, they can be judiciously sectioned to maximize the number of sections cut from an array. The sectioning process uses a tape-based sectioning aid (from Instrumedics Inc., Missouri, USA, *www.instrumedics.com*) that allows cutting of thinner sections. Optimal sectioning of arrays is obtained with about 2-3 μm sections. Thus, instead of 50-100 conventional sections or samples for analysis from one tissue biopsy, the microarray technique could produce material for 500 000 assays (assuming 250 biopsies per section times 2000 2.5-μm sections per 5 mm array block) represented as 0.6 mm disks of tissue. Thus this technique essentially amplifies (up to 10 000 fold) the limited tissue resource.[15]

Simultaneous analysis of very large numbers of specimens. Tissue microarrays provide high throughput data acquisition. For instance, if a tissue microarray block containing 1000 cores is cut 200 times, this allows for 200 000 individual assays.[19,20]

Experimental uniformity. With this technology, each tissue sample is treated in an identical manner and microarrays are amenable to a wide range of techniques, including histochemical stains, immunologic stains with either chromogenic or fluorescent visualization, in situ hybridization (including both mRNA ISH and FISH), and even tissue micro-dissection techniques. For each of these protocols, conventional procedures can have substantial slide-to-slide variability associated with processing 300 slides (for example, 20 batches of 15 slides). Tissue microarray allows the entire cohort to be analyzed in one batch on a single slide. Thus, variables such as antigen retrieval, temperature, incubation times, washing procedure, and reagent concentration are standardized for the entire cohort.[21-23]

Decreased assay volume, time and cost. As only a very small amount of reagent (a few μL) is required to analyze an entire cohort, less laboratory personnel are required to perform the experiments. This method has proven to be extremely efficient, of shorter duration, and cost effective, especially with expensive reagents.[4] This advantage raises the possibility of use of tissue microarrays in screening procedures.

Does not destroy original block for diagnosis and thus conserves valuable tissue. There are occasions where the original block must be returned to the patient or donating institution. In these cases the block may be cored a few times without destroying the original tissue block. Then, upon subsequent sectioning, it is still possible to make a diagnosis, even though tissue has been taken for array-based studies.

Tissue microarray has proved to be an effective and efficient tool for assessing quality assurance programs such as intra- and interlaboratory variation in immunohistochemical and molecular studies. A tissue microarray block can be created from numerous tissue specimens, then sectioned and unstained slides distributed to different laboratories, with each laboratory doing immunostains or molecular tests. Thus, tissue microarray can facilitate the standardization of immunohistochemical, fluorescence in situ hybridization, and other molecular assays, so that results are reproducible between laboratories. The tissue microarray also can be used in internal quality control (eg, quarterly or monthly) to ensure that there is no drift of staining results or reporting within a laboratory. It can also be used for optimization of diagnostic reagents such as monoclonal antibodies and gene probes.[5] It is believed that the tissue microarray is an improvement over the current practice of using a single strong positive control for quality.[24-26]

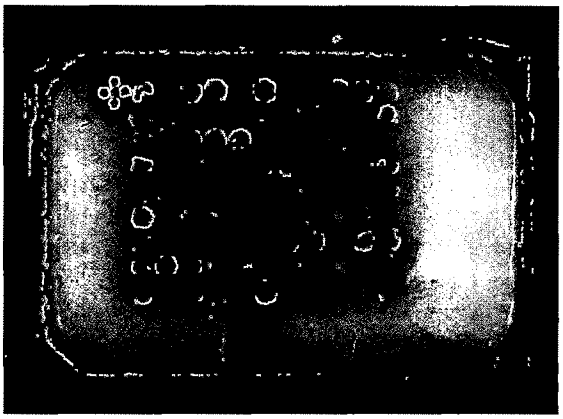

Figure 2. Tissue microarray block.

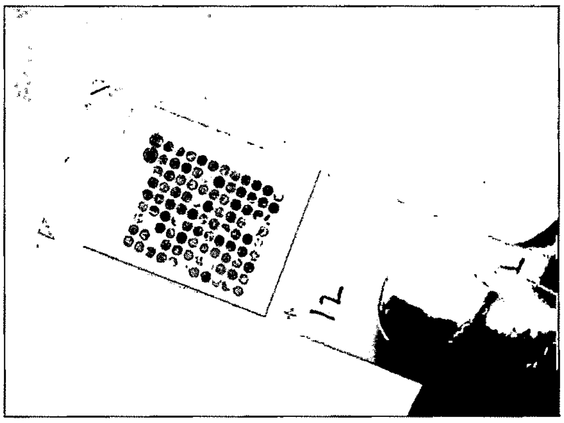

Figure 3. A tissue microarray slide.

Tissue microarray facilitates rapid translation of molecular discoveries to clinical applications. The technique has been applied to tumor research (gliomas, breast tumors, lung cancer among others). The development of novel biochip technologies has opened up new possibilities for the high-throughput molecular profiling of human tumors. Novel molecular markers emerging from high-throughput expression surveys can be analyzed on tumor tissue microarray.[27] Newly identified genes require clinical validation on histopathological specimens for any meaningful outcome. Such validation is best achieved by tissue microarray, as is seen in the analysis of tumor specimens. Depending on this, three categories of tissue microarray can be defined:[4] (1) With multitumor arrays, many tumor types are sampled, from a diverse set of donor blocks, and arrayed on one recipient tissue microarray block. With this type of tissue microarray, a large group of tumors can then be expeditiously screened for the presence or absence of novel markers.[28-30] (2) For tumor progression arrays, morphological and molecular changes through the different stages of tumor progression, of one particular tumor type, can be assessed in tumor progression tissue microarrays. In prostate cancer, for example, construction of such an array would involve sampling of normal prostate, benign prostatic hyperplasia, prostatic intraepithelial neoplasia and different stages of prostate cancer, from localized disease to metastatic cancer. In one of the most significant papers on prostate cancer recently, a tumor progression array was used to show that the expression of a novel protein, EZH2, correlated with aggressiveness of disease.[31] (3) In prognostic (patient outcome) arrays, correlation of tissue microarray-derived data with clinical follow-up, to assess prognosis or patient outcome, is of significant interest to clinicians and their patients.[4] An example is the study of the expression of the EZH2 protein in prostatic cancer. Beside its benefit as a marker of prostate cancer progression, it was shown that the degree of expression of this protein was related to outcome after radical prostatectomy.[31] Whilst strong expression was associated with recurrence of tumor after surgery in a third of patients, weak EZH2 staining was found in only 9% of individuals with clinical failure. Similar associations have been described in other neoplasms.[32-34]

Tissue heterogeneity and other disadvantages of tissue microarray

One of the most common criticisms of tissue microarray is that the small cores sampled may not be representative of the whole tumor, particularly in heterogenous cancers such as prostate adenocarcinoma and Hodgkin lymphoma.[4,13] However, many groups have shown excellent concordance between tissue microarray spots and whole sections in immunohistochemical studies of multiple tumor types. Comparing the results of whole tissue sections with that of tissue microarray in quality assessment of estrogen receptor status in breast cancer, Parker et al found the results of microarray core for estrogen receptors (ie, positive vs negative) were the same as the results of the whole sections of the tumors in 96% of cases.[24] Another study that examined validation of tissue microarray technology for immunohistochemical assays, found that the analysis of two core sections from one case was comparable to the analysis of whole tissue sections in more than 95% of cases.[35] A third study of more than 2000 bladder cancers assessed for histologic grade and proliferative index, information obtained from four 0.6-mm cores per case was highly concordant with that obtained from the whole sections.[36] These findings demonstrate that intratumoral heterogeneity should not be a major impediment to use of arrays in quality assurance studies. Another minor disadvantage includes the absence of one or more core sections on the immunostained slide.[24] Although any given histo-spot may be negative or absent on a given array, the statistical power of analysis of hundreds or thousands of cases eliminates the affect of variability of a single data point in the ultimate conclusions.[15]

Automation

Attempts have been made to automate the process of tissue microarray construction. Various machines are now available (automated tissue arrayer) which may array single and multiple tissue microarray blocks in an even shorter period of time than that performed manually.[37] Furthermore, digital techniques have taken center stage in clinical medicine as well as in biomedical research. Recently pathology has begun to embrace this digital revolution. The first development was a high throughput microscopic slide scanner that can convert traditional glass microscopic slides into digital images that can be stored, retrieved, shared through the internet and, most importantly, algorithmically analyzed. The other development was the creation of algorithms that can identify and quantitate immunohistochemical staining patterns and specific histological features, such as nuclear size and mitosis. Such an algorithm can be applied to digital images of microarray. Digital pathology and imaging technology that can scan tissue microarrays into "virtual slides" with high resolution and that can analyze their images algorithmically will accelerate the discovery of new predictive biomarkers.[38]

Conclusion

Tissue microarray is a practical and effective tool for high-throughput molecular analysis of tissues that is helping identify new diagnostic and prognostic markers and targets in human cancers. It has varying degrees of research use and offers a range of potential applications in basic research, prognostic oncology and drug discovery. It is anticipated that tissue microarray will soon become a widely used tool for all types of tissue-based research. Tissue microarray technique will lead to a significant acceleration in the transition of basic research findings into clinical applications.

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brief report

Knowledge, attitudes and prevalence of tobacco use among physicians and dentists in Oman

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Ann Saudi Med 2009; 29(2): 128-133

Tobacco use among Omani physicians and dentists has not been studied, so we conducted a cross-sectional survey using a WHO questionnaire to measure prevalence and to learn about smoking practices among this population and about their knowledge and attitudes of the health effects of tobacco use and tobacco control. The 1191 subjects who participated (787 men and 404 women) ranged in age from 24 to 65 years with a mean (SD) of 41.7 (6.8) years for men and 38.1 (6.9) years for women. The prevalence of tobacco use was 16.4% among males and less than 1% among females. Manufactured cigarettes were the most common form of tobacco used (14.7%), followed by smokeless tobacco (2.2%) and waterpipes (1.7%). Tobacco users were significantly less favorable to strict control and policy measures than never tobacco users and had less knowledge of some of the heatlh effects of tobacco use. Tobacco use among physicians and dentists in Oman is lower than in other countries in the region, but remains a cause of concern. Programs and policies should strive to maintain the low level of tobacco use or reduce it further.

Tobacco is the second major cause of death and fourth most common risk factor for disease worldwide.[1] Health professionals often fall victim to this addiction even before embarking on a career in health care. Since tobacco use among Omani physicians and dentists has not been studied, we conducted a cross-sectional study to measure prevalence and gathered information on smoking practices and knowledge and attitudes on the health effects of tobacco use and tobacco control.

SUBJECTS AND METHODS

The target group for this survey was all physicians and dentists employed by the Ministry of Health in Oman. The sample size was calculated based on the prevalence of smoking in the general population of 24% in males and 2% in females.[2] Considering a non-response rate of 30% and a precision of 8% on either side of the 95% confidence interval for any point estimate, the sample size was estimated to be 1231 males and 769 females (Epinfo version 6; CDC, Atlanta, GA, USA). The questionnaire, The World Health Organization Global Health Professional Survey (see Appendix), was self-administered anonymously by each selected physician and dentist. Knowledge, attitudes and cessation counseling practices were assessed on an ordinal 5-points Likert scale where each response was ranked by giving equally spaced weight: 1, strongly agree; 2, agree; 3, unsure; 4, disagree; 5, strongly disagree. Prevalence estimates were calculated using Intercooled Stata software (version 9.1, Stata Corporation, College Station, Texas, USA, *http://www.stata.com*). Differences between mean responses of never and ever tobacco users were calculated using two independent samples *t* test. The closer the mean score of all the respondents to one, the stronger their agreement with the proposed statement. Differences were considered to be statistically significant if the *P* value was <.05.

A daily tobacco user was defined as someone who used tobacco products at the time of the survey at least once a day. An occasional smoker was someone who smoked at the time of the survey but not every day. Both of these categories were combined to give "current smoker". When other forms of tobacco use were added,

Table 1. Current and ex-smokers by type of tobacco used, and specialty among physicians and dentists (n=1191) in Oman, 2001.

	Omani (n=134)		Non-Omani (n=1057)		Total
	Male (n=73)	Female (n=61)	Male (n=714)	Female (n=343)	
All types of tobacco					
Current users	8 (11.0)	1 (1.6)	121 (17.0)	2 (0.6)	132 (11.1)
Ex-users	6 (8.2)	0 (0.0)	125 (17.5)	4 (1.2)	135 (11.3)
Cigarettes					
Current users	8 (11.0)	0 (0.0)	108 (15.1)	2 (0.6)	118 (9.9)
Ex-users	6 (8.2)	0 (0.0)	136 (19.0)	4 (1.2)	146 (12.3)
Waterpipes					
Current users	1 (1.4)	1 (1.6)	12 (1.7)	0 (0.0)	14 (1.2)
Smokeless tobacco					
Current user	0 (0.0)	1 (1.6)	17 (2.4)	1 (0.3)	19 (1.6)
Specialty					
General practicioners (n=326)	4 (18.2)	1 (4.0)	66 (35.3)	2 (2.1)	73 (22.4)
Medical (n=411)	4 (16.0)	0 (0.0)	87 (31.0)	3 (3.2)	94 (22.9)
Surgical (n=317)	4 (26.7)	0 (0.0)	66 (36.5)	0 (0.0)	70 (22.1)
Laboratory** (n=25)	0 (0.0)	0 (0.0)	3 (42.8)	0 (0.0)	3 (12.0)
Dental (n=48)	1 (20.0)	0 (0.0)	11 (42.3)	0 (0.0)	12 (25.0)

Values are number of subjects and percentage of column total for type of tobacco use or total for each specialty. Note: In 3 subjects the nationality was unknown and they were excluded in the above analysis. In 64 subjects the specialty was unknown but they were included in the overall analysis. No attempt was made to identify ex-users of waterpipes and smokeless tobacco. *Laboratory physicians e.g. pathologists or microbiologists.

the category was labelled as "current tobacco users". An ex-smoker was someone who smoked daily or occasionally or someone who smoked at least 100 cigarettes in his lifetime, but did not smoke at the time of the survey. A never-smoker was someone who never smoked at all or had never been a daily smoker or had smoked less than 100 cigarettes up to the time of the survey. Permission to conduct the study was obtained from the research and ethical committee of the Ministry of Health of Oman.

RESULTS

Of the 2021 physicians and dentists invited to participate, 119 (58 men and 61 women) were found to have resigned and left the country. Of the remaining 1902 physicians and dentists, data from 1191 subjects were analyzed (787 men and 404 women). The number of subjects was lower than the calculated sample size due to the moderate response rate. The response rate was higher in men (67.1%) than in women (55.4%). Participant age ranged from 24 to 65 years. The mean (SD) age was 41.7 (6.8) years for men and 38.1 (6.9) years for women. Over 84% of physicians (n=1079) and dentists (n=48) were aged between 30-49 years. Eleven percent were Omani nationals, 29% were general practitioners, 36% were internists, 28% surgeons, 4% dentists and 2.2% were laboratory physicians.

Tobacco use was more prevalent among non-Omani males aged 30-49 years. Overall, 16.4% (129/787) of males and less than 1% (3/404) of females were current users of any form of tobacco (Table 1). The prevalence of current tobacco use among Omani males was 11% (8/73) compared to 17% (121/714) in non-Omanis (P=0.188). Manufactured cigarettes were the most common form of tobacco used by males (14.7%) (116/787) followed by smokeless tobacco (nasal snuff, oral snuff and chewing tobacco and betel quid) (2.2%) (17/787) and waterpipes (1.7%) (13/787).

There were statistically significant differences in physician and dentist perception of clinical practice and attitudes towards tobacco control polices (Table 2). Tobacco users were significantly less favorable to strict control and policy measures than never tobacco users and had less knowledge of some of the health effects of tobacco use.

Table 2: Comparison of knowledge and attitudes of physicians and dentists towards tobacco control, Oman, 2001.

Statement	Mean score		*P* value
	Never used tobacco	Ever used tobacco	
Patient's chances to quit are increased if a health professional advises them so	1.9	2.1	.001
Health professionals should routinely ask about their patients smoking habits.	1.6	1.7	.046
Heath professionals should routinely advise their smoking patients to quit smoking.	1.5	1.6	.004
Health professionals who smoke are less likely to advise people to stop smoking.	2.1	2.7	.001
Health professionals should get specific training on cessation techniques.	1.7	1.9	.002
Smoking in enclosed public places should be prohibited.	1.1	1.3	.001
Health warnings on cigarette packages should be in big print.	1.3	1.5	.001
Tobacco sales should be banned to children and adolescents.	1.1	1.2	.092
Sport sponsorships by tobacco industry should be banned.	1.5	1.6	.390
There should be a complete ban on the advertising of tobacco products.	1.5	1.7	.019
Hospitals and health care centers should be "smoke-free".	1.1	1.2	.007
The price of tobacco products should be increased sharply.	1.7	2.2	.001
Maternal smoking during pregnancy increases the risk of SIDS*	1.7	1.9	.012
Passive smoking increases the risk of lung disease in non-smoking adults.	1.5	1.7	.001
Passive smoking increases the risk of heart disease in non-smoking adults.	1.8	1.9	.104
Paternal smoking increases the risk of lower respiratory tract illnesses such as pneumonia in exposed children.	1.8	1.9	.015

*SIDS, Sudden infant death syndrome

DISCUSSION

This study documents for the first time, the prevalence of tobacco use, knowledge of and attitudes towards tobacco control among physicians and dentists working in Oman. The study shows that tobacco use is predominantly a male disease and that its use among Omani physicians and dentists is relatively low (11%) compared to the general population (24%).[2] In 1995, Sulaiman et al reported that the prevalence of any current tobacco use among Omanis aged 15 years and above, in the general population, was 15.5% in males and 1.5% in females.[3] A second community-based survey (in 2000) among Omanis aged 20 and above, reported similar figures for current smokers (13.4% males and 0.5% females).[4]

Using an identical questionnaire and methodology, higher rates of tobacco use were reported among physicians and dentists from other Arab countries such as the United Arab Emirates (43%), Kuwait (31%), Bahrain (23%), Libya (17.2%), Saudi Arabia (14.2%) and Qatar (12%).[5-7] The low prevalence rates of tobacco use in Oman have been a consistent finding when compared to other Arabian Gulf states. This may be attributed to the fact that Oman's renaissance, which opened it to world markets, including the tobacco trade, occurred at least a decade later (in the 1970s following commercial exploitation of oil and a régime change) than other Gulf states. Further, tobacco use has been traditionally a taboo in Oman's non-coastal areas, in congruence with the strict ruling by the religious authorities (the Abadhi sect of Islam in Oman) that have long declared tobacco use as haram (religiously forbidden).

Although waterpipe smoking is emerging as a fashionable mode of tobacco use in the Arab world,[8] its use among physicians and dentists in Oman was extremely rare (1.2%). This could be because it is not so easy to use (compared to smoking cigarettes). Media advertisement for cigarettes could also have tipped the balance in favor of cigarettes considering there are none or rarely any advertisements for waterpipes.

Our results show a high prevalence of tobacco use among dentists. While this could be due to the small sample size of this group, other studies have also shown a higher prevalence of tobacco use among dentists compared to physicians of other specialties.[9,10] In addition, the percentage of Omani doctors and dentists in the Ministry of Health is about 24% while in our study it was 10% because we selected a sample from all males disregarding the stratification of Omanis and non-Omanis. For females, the calculated sample size was nearly the same as the total number of female dentists and doctors working in the Ministry of Health.

Physicians and dentists, who had used or currently use tobacco, were less approving of evidence-based measures to control tobacco than never users. This finding is consistent with other studies where smokers report less support for tobacco control measures than non-smokers.[11] However, it must be cautioned that not all smokers are homogeneously opposed to all tobacco control polices.[12]

There were a few limitations to this study. The low response rate among female physicians and dentists could be attributed to the social taboo and unacceptability of tobacco use among women in oriental societies, including Omanis. Low female participation has also been reported from similar studies across other Arab nations (Jordan 13%, Saudi Arabia 21%, Egypt 24%, Qatar 28%, Libya 41%) compared to 34% in Oman.[13] Our survey has excluded physicians and dentists working in police and army hospitals as well as private sector clinics. We estimated this group to be around 25% to 30% of all the physicians and dentists working in the country.

We conclude that tobacco use among physicians is a cause for concern, more so among non-national physicians and dentists than among Omanis. Efforts should capitalize on this finding and programs and polices should strive to maintain this low level of tobacco use or reduce it even further.

Acknowledgments

We would like to thank the following persons for their cooperation and support without which the study would not have been possible: Dr. Hani Naguib, Dr. Mohammed Redha, Dr Ahmed Tahir Ba Omar Dr Mohammed Hassan, Dr Halima Hinai, Dr Magdi Abdul Hafidh, Dr Abduleillah Al-Geilani, Dr Riyadh Hassan Mohammed, Dr Ashraf Mahmood Marei, Dr Louis Yessi Zaki, Dr Amal Hamid Abdullah, Dr. Mohammed Shibara and Mr. Yousef Al-Thuhli.

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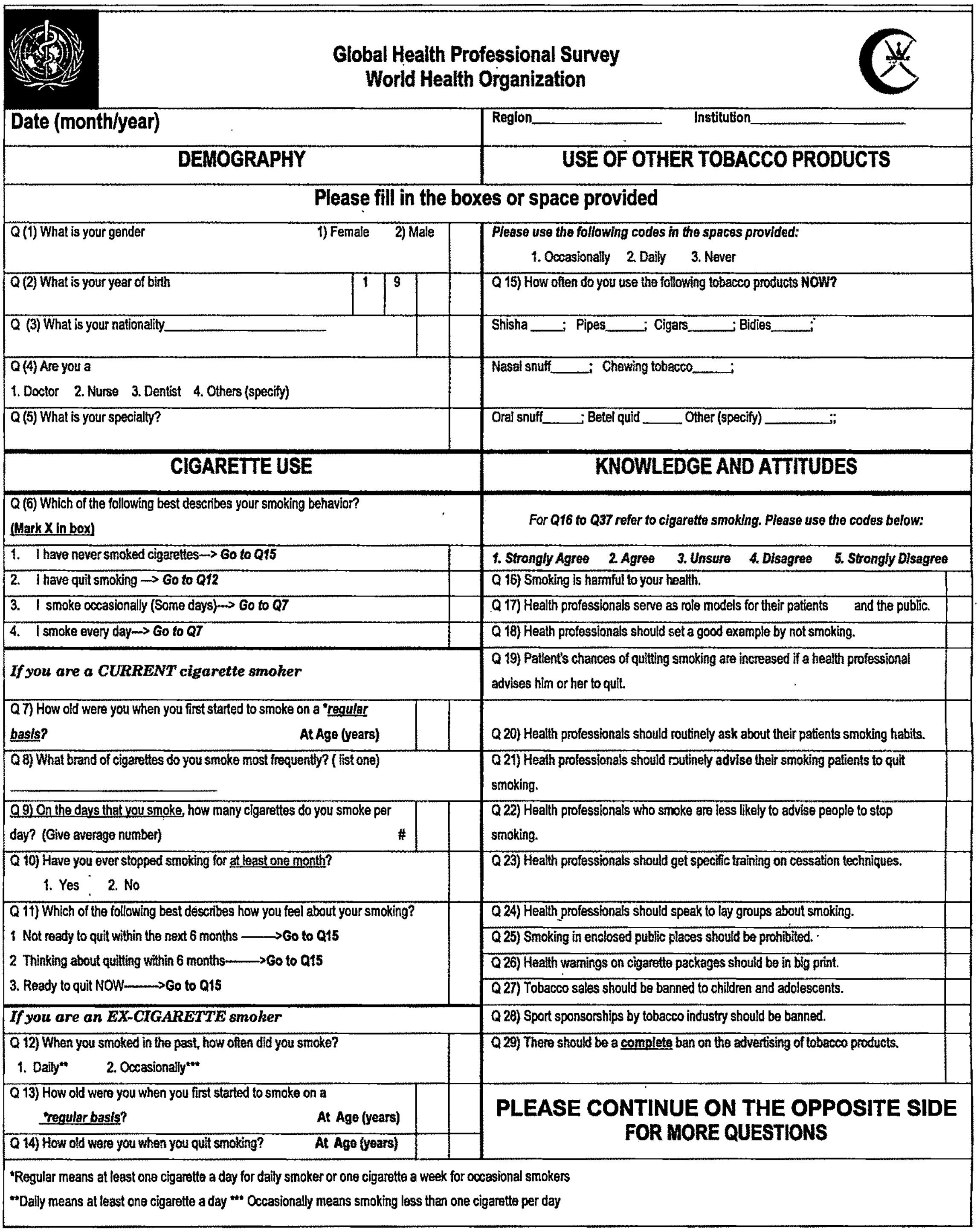


Global Health Professional Survey
World Health Organization

Date (month/year)

Region_______________ **Institution**_________________

Please fill in the boxes or space provided

DEMOGRAPHY

Q (1) What is your gender 1) Female 2) Male

Q (2) What is your year of birth 1 9

Q (3) What is your nationality______________________

Q (4) Are you a
1. Doctor 2. Nurse 3. Dentist 4. Others (specify)

Q (5) What is your specialty?

CIGARETTE USE

Q (6) Which of the following best describes your smoking behavior?
(Mark X in box)

1. I have never smoked cigarettes—> *Go to Q15*
2. I have quit smoking —> *Go to Q12*
3. I smoke occasionally (Some days)—> *Go to Q7*
4. I smoke every day—> *Go to Q7*

If you are a CURRENT cigarette smoker

Q 7) How old were you when you first started to smoke on a *__regular basis__? **At Age (years)**

Q 8) What brand of cigarettes do you smoke most frequently? (list one)
____

Q 9) __On the days that you smoke__, how many cigarettes do you smoke per day? (Give average number) #

Q 10) Have you ever stopped smoking for __at least one month__?
1. Yes 2. No

Q 11) Which of the following best describes how you feel about your smoking?
1 Not ready to quit within the next 6 months ———>**Go to Q15**
2 Thinking about quitting within 6 months———>**Go to Q15**
3. Ready to quit NOW———>**Go to Q15**

If you are an EX-CIGARETTE smoker

Q 12) When you smoked in the past, how often did you smoke?
1. Daily** 2. Occasionally***

Q 13) How old were you when you first started to smoke on a *__regular basis__? **At Age (years)**

Q 14) How old were you when you quit smoking? **At Age (years)**

USE OF OTHER TOBACCO PRODUCTS

Please use the following codes in the spaces provided:
1. Occasionally 2. Daily 3. Never

Q 15) How often do you use the following tobacco products **NOW?**

Shisha_____; Pipes_____; Cigars______; Bidies______;

Nasal snuff______; Chewing tobacco______;

Oral snuff______; Betel quid ______ Other (specify) __________;;

KNOWLEDGE AND ATTITUDES

For Q16 to Q37 refer to cigarette smoking. Please use the codes below:

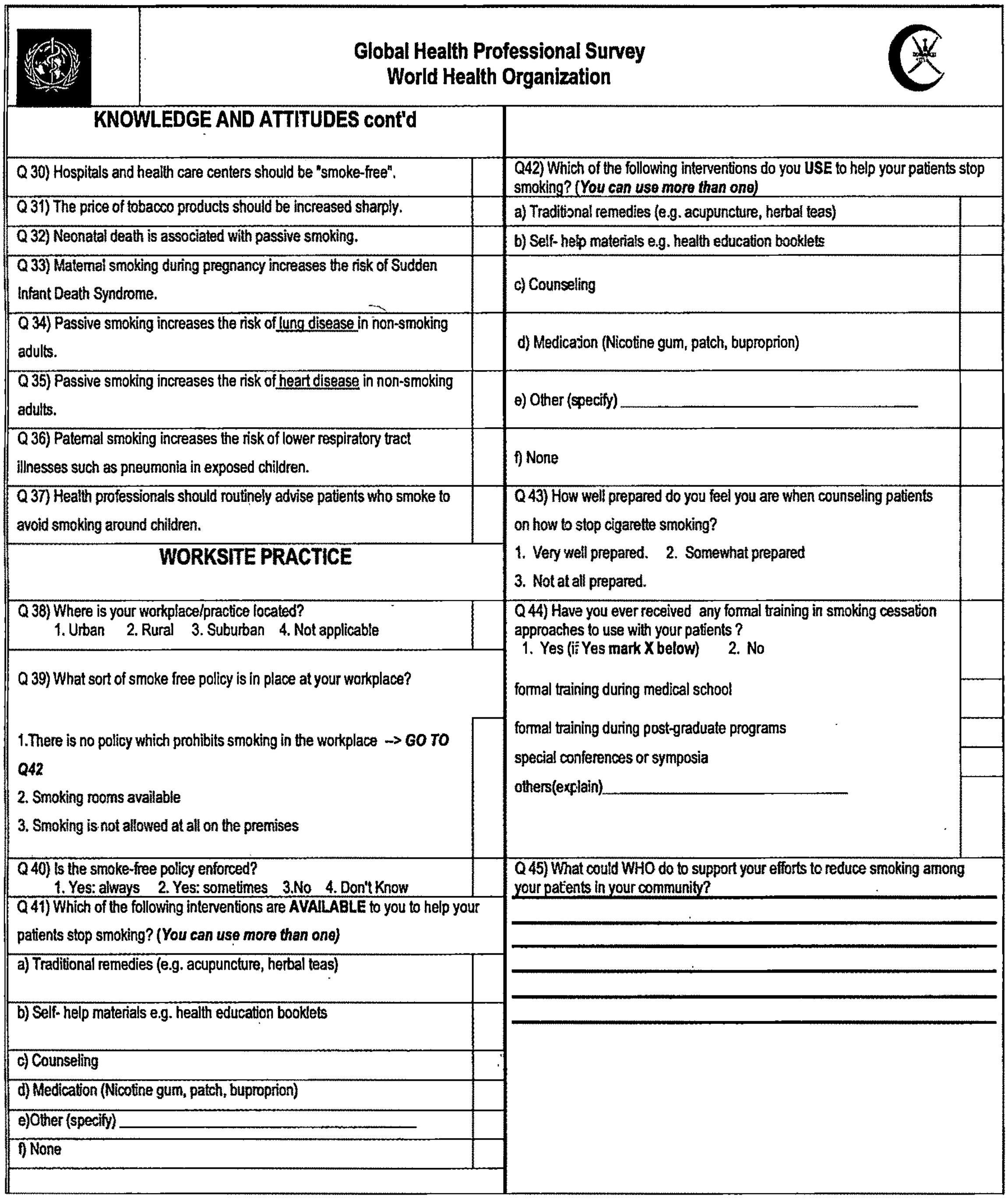
1. Strongly Agree 2. Agree 3. Unsure 4. Disagree 5. Strongly Disagree

Q 16) Smoking is harmful to your health.
Q 17) Health professionals serve as role models for their patients and the public.
Q 18) Heath professionals should set a good example by not smoking.
Q 19) Patient's chances of quitting smoking are increased if a health professional advises him or her to quit.
Q 20) Health professionals should routinely ask about their patients smoking habits.
Q 21) Heath professionals should routinely advise their smoking patients to quit smoking.
Q 22) Health professionals who smoke are less likely to advise people to stop smoking.
Q 23) Health professionals should get specific training on cessation techniques.
Q 24) Health professionals should speak to lay groups about smoking.
Q 25) Smoking in enclosed public places should be prohibited.
Q 26) Health warnings on cigarette packages should be in big print.
Q 27) Tobacco sales should be banned to children and adolescents.
Q 28) Sport sponsorships by tobacco industry should be banned.
Q 29) There should be a __complete__ ban on the advertising of tobacco products.

PLEASE CONTINUE ON THE OPPOSITE SIDE FOR MORE QUESTIONS

*Regular means at least one cigarette a day for daily smoker or one cigarette a week for occasional smokers
Daily means at least one cigarette a day * Occasionally means smoking less than one cigarette per day

Appendix. World Health Organization Global Health Professional Survey.



Global Health Professional Survey
World Health Organization

KNOWLEDGE AND ATTITUDES cont'd

Q 30) Hospitals and health care centers should be "smoke-free".

Q 31) The price of tobacco products should be increased sharply.

Q 32) Neonatal death is associated with passive smoking.

Q 33) Maternal smoking during pregnancy increases the risk of Sudden Infant Death Syndrome.

Q 34) Passive smoking increases the risk of lung disease in non-smoking adults.

Q 35) Passive smoking increases the risk of heart disease in non-smoking adults.

Q 36) Paternal smoking increases the risk of lower respiratory tract illnesses such as pneumonia in exposed children.

Q 37) Health professionals should routinely advise patients who smoke to avoid smoking around children.

WORKSITE PRACTICE

Q 38) Where is your workplace/practice located?
1. Urban 2. Rural 3. Suburban 4. Not applicable

Q 39) What sort of smoke free policy is in place at your workplace?

1.There is no policy which prohibits smoking in the workplace --> ***GO TO Q42***
2. Smoking rooms available
3. Smoking is not allowed at all on the premises

Q 40) Is the smoke-free policy enforced?
1. Yes: always 2. Yes: sometimes 3.No 4. Don't Know

Q 41) Which of the following interventions are **AVAILABLE** to you to help your patients stop smoking? ***(You can use more than one)***

a) Traditional remedies (e.g. acupuncture, herbal teas)
b) Self- help materials e.g. health education booklets
c) Counseling
d) Medication (Nicotine gum, patch, buproprion)
e)Other (specify) ____________________
f) None

Q42) Which of the following interventions do you **USE** to help your patients stop smoking? ***(You can use more than one)***

a) Traditional remedies (e.g. acupuncture, herbal teas)
b) Self- help materials e.g. health education booklets
c) Counseling
d) Medication (Nicotine gum, patch, buproprion)
e) Other (specify) ____________________
f) None

Q 43) How well prepared do you feel you are when counseling patients on how to stop cigarette smoking?
1. Very well prepared. 2. Somewhat prepared
3. Not at all prepared.

Q 44) Have you ever received any formal training in smoking cessation approaches to use with your patients ?
1. Yes (if Yes **mark X below**) 2. No

formal training during medical school
formal training during post-graduate programs
special conferences or symposia
others(explain)____________________

Q 45) What could WHO do to support your efforts to reduce smoking among your patients in your community?

Appendix (cont.). The World Health Organization Global Health Professional Survey.

brief report

The accuracy of ultrasonography in the diagnosis of superficial bladder tumors in patients presenting with hematuria

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Ann Saudi Med 2009; 29(2): 134-137

Ultrasonography has been proposed as the initial test for detection of bladder carcinomas in patients presenting with hematuria, but the accuracy of transabdominal ultrasonography in the diagnosis of superficial bladder carcinoma has not been assessed. We prospectively evaluated 173 patients presenting to the outpatient department with painless hematuria by transabdominal ultrasound and cystoscopy. The tolerability of cystoscopy was also assessed. Of 148 patients who met the inclusion criteria, 39 with bladder carcinoma were identified by cystoscopy as having bladder carcinoma, while 34 were identified by ultrasonography. For ultrasonography, the sensitivity (87.1%), specificity (98.1%), positive predictive value (94.4%) and negative predictive value (95.4%) were good but not as good as cystoscopy. While the tolerability of cystoscopy is relatively low, it is still superior to ultrasonography in the evaluation of the bladder as a possible source of hematuria.

Painless hematuria usually is the sole presenting symptom in the majority of patients with bladder cancer.[1] Therefore, painless hematuria of any degree in adults should be regarded as a symptom that is suspicious for malignancy until proved otherwise. Cystoscopy is considered the gold standard in the evaluation of hematuria.[2] This technique directly visualizes lower urinary tract anatomy and macroscopic pathology, which may be responsible for the clinical picture under evaluation. However, cystoscopy is invasive, time-consuming and expensive.[3]

Currently, modern sensitive transducers have improved imaging of the urinary tract and therefore transabdominal ultrasound is more effective in visualizing intra-luminal filling defects in the bladder than it was in the past. Moreover, ultrasonography is a non-invasive, well-accepted, and cost-effective diagnostic procedure. Systematic use of ultrasonography has been proposed as the initial test for detection of bladder carcinomas in patients presenting with hematuria.[4] The present study was carried out to investigate prospectively the accuracy of modern transabdominal ultrasonography in the diagnosis of superficial bladder carcinoma. The tolerability of cystoscopy was also measured. To our knowledge, no trials have compared the accuracy of modern ultrasound devices with cystoscopy in the diagnosis of superficial bladder carcinoma and only a few studies have given attention to the tolerability and acceptance of urological endoscopic procedures by patients.[5-8]

PATIENTS AND METHODS

In this controlled prospective study, which took place at the General Hospital of Thebes (Viotia, Greece) from April 2006 to January 2008, 173 consecutive patients who presented with painless hematuria; microscopic (n=108) and macroscopic (n=65) were asked to participate. Only those patients who had an established diagnosis of hematuria (>10 red blood cells in the urinalysis) were included in the study. Patients with microscopic hematuria were all referred by internists. Their complaints were a sensation of burning during urination, lower urinary tract symptoms, loss of weight, anemia and persistent fever. Patients with painless macroscopic hematuria had no other symptoms. Patients eligible for the study were those with a new diagnosis of hematuria who were able to undergo cystoscopy. Patients who did not agree to undergo cystoscopy as well as those with an established history of recurrent superficial bladder cancer and/ or carcinoma in situ were excluded from the study. Eligible patients had a urinary tract abdominal ultrasound examination performed with a full bladder. Urinary tract ultrasonography was performed by two consultant radiologists. The examination was performed with a convex 2.5-5 MHz transducer. A linear 5-7.5 MHz transducer was also used to visualize defects of the bladder dome. (LOGIQ 3 Pro, General Electric Ultraschall, Beethovenstraße 239, Solingen, Germany). Patients who presented with blood casts in the urine sample underwent transurethral catheterization and bladder lavage. Eight patients who presented with serious hematuria that did not respond to bladder lavage underwent Color or spectral Doppler ultrasound investigation. The bladder was examined with several different transducers to maximize the likelihood of detection of small lesions. High frequency curved arrays were used to scan the bladder dome. Duplex/CFD was used to determine if a bladder mass was vascularized and therefore arising from the wall in some cases. The main diagnostic criterion for the ultrasonographic diagnosis of superficial bladder cancers was the presence of irregular soft tissue structures of low- to intermediate-echo texture projecting into the bladder lumen from a fixed mural site. Two consultant urologists, who were blinded to the ultrasound results, with an Olympus rigid cystoscope performed cystoscopy.The two urologists performed cytoscopy on the same patient in the two different sessions, and therefore were not aware of the results of the other. A uniform registration form was used for recording findings of ultrasound and cystoscopy from each patient. At the end of the study, the reported findings of urinary tract ultrasonography were correlated with those visualized by cystoscopy. The tolerability of cystoscopy was self-estimated and recorded: each patient was provided with an optical pain-meter scaled from 0 to 10 to measure discomfort or pain level of cystoscopy. Pain-Meter is a self-administered pain assessment tool developed in 1996 for the purposes of improving assessment and management of pain in acute and chronic pain patients. The Pain-Meter (Lavipharm, Greece) used in our study is a hard, white tool that consist of a 10-cm visual analogue scale with a moveable marker that patients used to rate their pain.[9] Patients with ultrasound and/or cystoscopy suspicious for bladder carcinoma were further evaluated. Transurethral resection of the tumors and histopathological analyses were performed at Urology Department, Thriassio General Hospital, Elefsina, Greece and pathology Urology Department, Thriassio General Hospital, Elefsina, Greece respectively. Confirmation of the bladder carcinoma was achieved by histopathological examination of the submitted specimens of bladder biopsy in each case. The locally appointed ethics committee approved the research protocol, while all subjects were informed and consented to participation. The administration of the General Hospital of Thebes provided financial support.

RESULTS

Of 148 patients (53 women and 95 men) finally included, all underwent ultrasound examination. Twenty-five patients were excluded from the study (13 refused cystoscopy, 3 were not suitable for undergoing cystoscopy, 7 had a history of recurrent bladder cancer and 2 were under treatment for carcinoma in situ). The male patients ranged in age from 33 to 85 years (median 63.2 years) while the female patients ranged in age from 34 to 76 years (median 58.6 years). The examination was interrupted in 7 of 40 patients due to limited tolerability of the cytoscopy procedure while the remaining 34 did not attend the second cytoscopy session. Thirty-nine patients were finally identified with bladder carcinoma by cystoscopy. In 34 patients (87.1%) ultrasonography accurately diagnosed tumor while in 5 patients it failed to clearly diagnose bladder carcinoma. More precisely, in one patient the bladder carcinoma was reported as a prostatic lobe and in another patient the tumor was located in a bladder diverticulum and was reported as a vesical stone. In the remaining three cases the bladder tumor was smaller than 3 mm. Two patients had a false-positive ultrasonographical diagnosis of bladder cancer. In both patients the intraluminal-filling defect was the median lobe of the hypertrophic prostate. In two cases, radiologists suggested different diagnoses (interobserver variation). Inter-observer variations recorded in the ultrasonography registration form were mainly differences in estimating the size and number, in the case of multiple tumors, as well as the localization of bladder tumors (Table 1).

The performance characteristics of ultrasonogra-

Table 1. Misdiagnoses of ultrasonography and cystoscopy in the detection of bladder carcinoma.

	Abdominal Ultrasound	Cystoscopy
Interobserver variations	2	2
False positive findings	2	1
False negative findings	5	1

Table 2. Evaluation of ultrasonography in the diagnosis of bladder carcinoma.

	Actual diagnosis		
Result	With disease	No disease	Totals
Positive	34	2	36
Negative	5	103	108
Totals	**39**	**105**	**144**

Sensitivity=87.1% (34/39), specificity=98.1%(103/105). Positive predictive value=94.4%(34/36), negative predictive value=95.4%(103/108).

phy in the diagnosis of bladder carcinoma are shown in Table 2. In 6 of the 39 patients with bladder carcinoma, an abnormality in the upper urinary tract was found (hydronephrosis and hydroureter secondary to ureteric involvement by bladder carcinoma), as well as renal pelvis stones and renal cysts. In two cases, interobserver variations in the cystoscopy registration form were only in the exact tumor size. In the case of carcinoma in situ one of the two urologists did not identify the presence of the tumor. Abnormalities resembling bladder cancer were described. Final diagnosis of cancer was established upon pathologic examination of the resected tissue.

The mean discomfort level of cystoscopy estimated by each patient on optical pain-meter was 5.74. This value was slightly higher when calculated only for men and slightly lower when calculated only for women. Differences in cystoscopy tolerability (ranged from 0-8 in males, 4-10 in females) between males and females were not of statistical significance.

DISCUSSION

Cystoscopy is currently the best test for evaluation of the bladder as a possible source of hematuria; however, as seen in our study, in rare cases cystoscopy may not reveal a tumor in the bladder.[2] Additionally, diagnostic cystoscopy is usually performed on an outpatient basis under local anaesthesia and is usually considered a painful diagnostic procedure. However, the tolerability and acceptance of diagnostic cystoscopy by patients has not been thoroughly documented. As seen from our study, the pain is moderately tolerated. Our findings are comparable to those of a few previous studies examining the tolerability and morbidity of other endoscopic procedures (eg. ureteroscopic lithotripsy under local anaesthesia, urodynamic studies etc).[4-7] In previous studies, differences in cystoscopy tolerability among male and female patients were attributed in these studies to the normal anatomical difference between the male and female urethra as well as by the additional difficulties in performing cystoscopy in male patients with enlarged prostates. Moreover, since routine pelvic gynecologic exams are usually performed annually among women of childbearing years it is plausible that women feel less discomfort than men when undergoing cystoscopy.

Technical and scientific advances in radiology have increased the diagnostic accuracy of imaging methods in the investigation of hematuria and various authors have proposed the use of imaging methods as the sole initial investigation for detection of bladder carcinomas in patients presenting with hematuria.[3] In fact, transabdominal ultrasonography is a simple and quick examination that can be safety performed on all individuals with no restrictions (for example, the elderly and handicapped patients that cannot undergo cystoscopy, and septic patients and those with renal failure that are contraindicated for intravenous pyelography). Ultrasonography is also easily available, cost-effective, and non-invasive, requiring no special preparation, and provides images of both the upper and lower renal tract. In the present study, ultrasonography accurately detected 87.1% of bladder carcinomas, while in 3 of 39 patients with bladder carcinoma, abnormalities not related to bladder carcinoma were also found, including renal pelvis stones (n=2), and renal cysts (n=1). In the past, the accuracy of ultrasound devices in the diagnosis of superficial bladder tumors was less than that of the current devices and this led to an underestimation of the value of ultrasound; thus, ultrasonography has been accused of not always being an appropriate method for the diagnosis of bladder cancer. Technological evolution has rendered current scanners, which combine several different transducers and color or spectral Doppler imaging facilities, more accurate in the visualization of intra-luminal filling defects of the bladder. In fact, detection rates for bladder carcinoma have been increased from 82% to 95%.[10,11] Despite remarkable improvements in the diagnostic accuracy, some of the pitfalls of ultrasonographic tests for evaluation of the bladder as a possible source of hematuria still remain. Smaller lesions (smaller than 0.5 cm) and lesions located in the dome or bladder neck are more difficult to visualize sonographically. Tumor configuration is also an important factor: plaque-like lesions are almost certainly harder to detect than polypoid ones.[11] Notably, in our study, the smallest carcinoma detected was 4 mm in size, while in 3 of 5 cases the ultrasound failed to detect bladder carcinoma for tumor sizes smaller than 3 mm. Note that the ultrasonography might lead to misdiagnosis due to external factors, such as obesity of patient and degree of bladder distension, while its adequacy depends on the experience and skill of the person performing the study.[10]

According to our findings, despite remarkable improvements in diagnostic accuracy, ultrasonography is still inferior to cystoscopy in the evaluation of the bladder as a possible source of hematuria and neither ultrasound nor the combination of urinary cytology and ultrasonography can replace the standard cystoscopic examination.[12]

Since the diagnosis of bladder cancer requires histopathological confirmation (on the core biopsy obtained during cystoscopy or of the bladder specimens obtained after Transurethral resection of the tumor) ultrasonography is certainly not the most adequate examination. However despite its own pitfalls it can provide a map of suspected areas to be further assessed by the following cystoscopy, while, the visualisation of a bladder tumour in earlier imaging -especially in small health settings where cystoscopy is not available - can save money and time. On the perspective of the authors, while endoscopic approach and biopsy remains the gold standard, ultrasonography represents a valuable tool in the initial radiological investigation for detection of bladder carcinomas. Patients presenting with painless hematuria should be initially investigated by ultrasound and -only if necessary- by cystoscopy in order to reach a complete diagnosis.

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case report

Amyloid goiter: two cases and a review of the literature

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Ann Saudi Med 2009; 29(2): 138-141

Although involvement of the thyroid gland by amyloid is a relatively common phenomenon, clinically significant enlargement of the thyroid owing to amyloid deposition is an extremely rare occurrence. We describe two cases of amyloid goiter and review the relevant literature. The first case was systemic amyloidosis secondary to familial Mediterranean fever. The second case was a chronic renal failure patient who presented with an enlarged thyroid and upper airway obstructive symptoms. To date, true amyloid goiter secondary to amyloidosis associated with familial Mediterranean fever has only been reported in twelve patients.

Although involvement of the thyroid gland by amyloid is a relatively common phenomenon, clinically significant enlargement of the thyroid owing to amyloid deposition is an extremely rare occurrence. We describe two cases of amyloid goiter and review the relevant literature. The first case was systemic amyloidosis secondary to familial Mediterranean fever. The second case was a chronic renal failure patient who presented with an enlarged thyroid and upper airway obstructive symptoms. To date, true amyloid goiter secondary to amyloidosis associated with familial Mediterranean fever has only been reported in twelve patients.

Amyloid goiter can be defined as the presence of amyloid within the thyroid gland in such quantities as to produce a clinically apparent enlargement of the gland. This unusual entity was first described in 1858 by Beckman, and in 1904 by Eiselberg, who advanced the name "amyloid goiter".[1,2] Focal microscopic deposition of amyloid within the thyroid gland might be seen in systemic secondary amyloidosis, medullary thyroid carcinoma and less frequently, in primary amyloidosis.[1,3] Clinically detectable thyroid enlargement from amyloid infiltration is rare, and most cases are not diagnosed prior to surgery. Amado et al reported 80 cases in a review of the world literature, most of which occurred in adults, although a few occurred in children.[4,5] To date, true amyloid goiter secondary to amyloidosis associated with familial Mediterranean fever (FMF) has only been reported in twelve patients.[6] The thyroid gland may be asymptomatically involved in most patients with systemic amyloidosis secondary to FMF. In this report, we describe two patients with amyloid goiter and we review the relevant literature.

CASE 1

A 16-year-old girl was diagnosed with FMF at the age of 10 years and was given colchicine. The patient was diagnosed as having secondary amyloidosis based on a renal biopsy performed to find out the cause of her clinical symptoms. On her last physical examination she had a bilateral, firm and diffusely enlarged thyroid gland. Her serum T3, T4, and TSH levels were all normal. A subtotal thyroidectomy was performed, with no complications. Grossly, the cut surface of the subtotal thyroidectomy material had a solid, white to pale-tan appearance and measured 8×6×3.5 cm. Microscopic examination by hematoxylin-eosin stained sections taken from both lobes of the thyroid revealed extensive infiltration of the parenchyma by an eosinophilic amorphous material consistent with amyloid substance (Figure 1). There was extensive fat cell metaplasia in the thyroid interstitium. The lining cells of the thyroid follicles were flattened and atrophic. There was no evidence of malignancy. Methyl violet stain was metachromatically positive in the involved tissue. This material stained intensely with Congo red and was apple green in color when examined microscopically under polarized light (Figure 2). Immunohistochemical staining patterns were consistent with amyloid AA (Clone mc1, Novocastra).

CASE 2

A 33-year-old male with secondary amyloidosis and chronic renal failure was admitted with rapidly growing goiter associated with hoarseness. Serum levels of the thyroid hormones and TSH were all normal. The patient underwent a subtotal thyroidectomy. The resected portion of the right lobe was enlarged and measured 10.5 cm in its greatest dimension. The resected portion of the left lobe was enlarged and measured 11 cm in greatest dimension. On gross examination of the thyroid gland, cut surfaces of both lobes of the thyroid had a largely solid, yellow-tan and irregular appearance. Both of the thyroid lobes were largely replaced by ill-defined solid, yellow-tan, fatty lesions. Microscopically, eosinophilic amorphous deposits were identified in interfollicular and perifollicular locations displacing and compressing the follicles. Areas of mature adipose tissue were seen intermixed with residual thyroid parenchyma and the eosinophilic amorphous deposits. Methyl violet stain was metachromatically positive in the involved tissue. These deposits stained intensely with Congo red and were apple green in color when examined microscopically under polarized light. Immunohistochemical evaluation demonstrated the presence of amyloid AA immunoreactivity (Clone mc1, Novocastra) (Figure 3).

DISCUSSION

Amyloidosis results from the deposition of insoluble, fibrous amyloid proteins, nearly always in the extracellular spaces of organs and tissues. Named by Virchow in 1854 on the basis of the color after staining with iodine and sulfuric acid, all amyloid proteins share a unique fibrillar ultrastructure. Depending upon the biochemical nature of the amyloid precursor protein, amyloid fibrils can be deposited locally or systemically, involving virtually every organ system of the body. Amyloid fibril deposition may have no apparent clinical consequences or may lead to severe pathophysiologic changes. Regardless of etiology, the clinical diagnosis amyloidosis is usually not made until the disease is far advanced.[7]

Amyloidosis can involve the thyroid as part of a systemic disease or as a localized primary amyloid tumor. Amyloid goiter is extremely rare and presents more frequently as an autopsy finding than in surgical material. The thyroid gland may be asymptomatically involved by amyloid substance in nearly 30% to 80% of patients with primary or secondary amyloidosis.[1,8] Amyloid substance might also be encountered in the thyroids of 50%

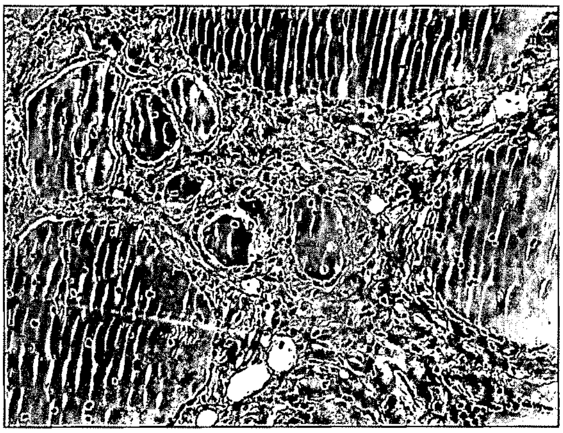

Figure 1. Diffuse eosinophilic amorphous material within interfollicular sites (hematoxylin-eosin, original magnification ×200).

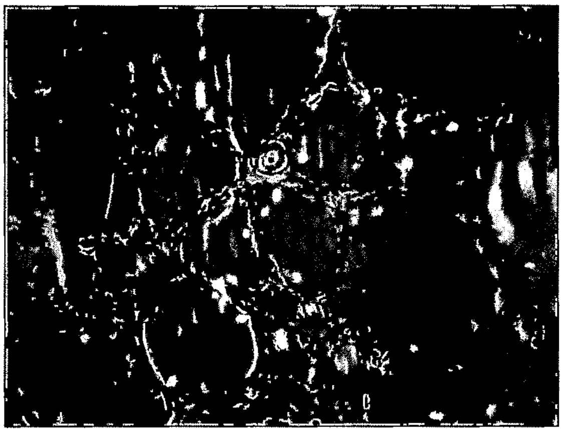

Figure 2. Methyl violet stain was metachromatically positive in the interfollicular sites (methyl violet, original magnification ×200).

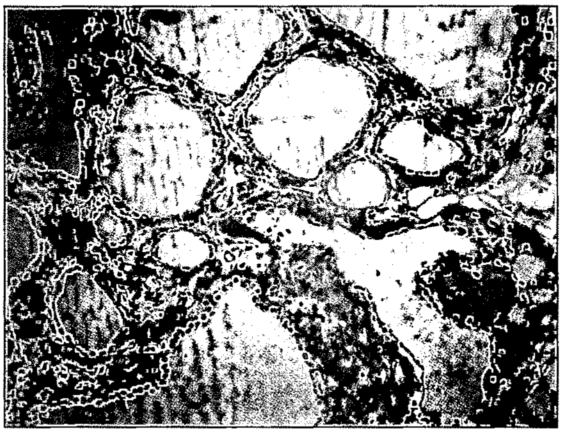

Figure 3. Immunohistochemically, eosinophilic material was positive with Amyloid AA (Avidin biotin, DAB Chromogen, original magnification ×200).

to 80% of patients with medullary thyroid carcinoma.[6] However, amyloid goiter, which is a symptomatic mass or clinically detectable thyroid enlargement due to amyloid deposition, is rare.[2] The lesion may be unilateral or bilateral and is commonly associated with a foreign body type reaction. The amyloid deposits are often accompanied by mature adipose tissue.[9] In the presented cases there was no foreign body type reaction, but in one patient extensive fat cell metaplasia in the thyroid interstitium was noted.

Amyloid goiter may be associated with either primary or secondary amyloidosis.[1] In Turkey, FMF is the most common cause of secondary amyloidosis. The most common clinical manifestation of FMF-related amyloid is the development of the nephrotic syndrome and eventually uremia.[10] However, the initial presence of a goiter caused by amyloid deposition is uncommon. Twelve cases of amyloid goiter complicating FMF were reported in the literature.[6] In one of our patients amyloid goiter was also associated with FMF. Most commonly amyloid goiter presents as a rapidly growing neck mass causing compression symptoms including dyspnea, dysphagia and/or hoarseness.[11] The enlargement of the gland is relatively rapid, occurring in weeks to several months. It usually presents as diffuse thyroid involvement, affecting both lobes, with a certain nodularity and associated firmness.[2] In our patients, one had a rapidly enlarged thyroid associated with hoarseness. The other patient was diagnosed with FMF with secondary amyloidosis and on her last physical examination she had a bilateral, firm and diffusely enlarged thyroid gland. Altparmak et al have reported three patients with amyloid goiter in FMF, although none of their patients had rapidly growing thyroids.[6]

The diagnosis of amyloid goiter should be considered in any patient with systemic amyloidosis presenting with an enlarging diffuse goiter and euthyroid state. In patients with amyloid goiter, thyroid function tests are often nonspecifically altered, and most patients are clinically euthyroid despite the diffuse involvement by the disease.[12] However, there are rare reports of patients with hypothyroidism or hyperthyroidism.[13,14] As previously stated, our patients had normal levels of T4, T3 and TSH.

The definitive diagnosis must be made by histologic evaluation of the resected thyroid gland, and although a fine needle aspirate may result in a definitive diagnosis, examination of resected tissue is usually necessary. Amyloid is usually present extracellularly as an amorphous, eosinophilic, proteinaceous substance in the light microscope. In cases of amyloid goiter, amyloid material is commonly seen infiltrating the parenchyma, distorting the normal tissue architecture. Other histologic features occurring in amyloid goiter include large foci of fatty metaplasia and rarely, squamous metaplasia as demonstrated by one of our patients as well. Histochemical stains aid in the confirmation of amyloid. These stains include Congo red, thioflavin T, and crystal violet stains. Congo red, the most frequently used technique, imparts a unique apple green birefringence when viewed under polarized light and is considered a pathognomonic feature of amyloid. Immunohistochemical techniques may help differentiating amyloid A from other types of amyloid.[2,15]

The presence of amyloid in the thyroid gland must raise the differential diagnosis of medullary carcinoma of the thyroid. In some cases amyloid may appear to almost completely obscure the underlying carcinoma. However, the lack of calcitonin reactive neoplastic cells and the presence of a background of C-cell hyperplasia can help to make this distinction. Amyloid deposition can also be seen in other conditions such as multiple myeloma, solitary plasmacytoma, infections, FMF, rheumatoid arthritis and a hyalinizing trabecular adenoma. However, these lesions each have a unique and different histologic appearance which renders discrimination easy.

The preoperative diagnosis of amyloid goiter should be suspected in patients with longstanding predisposing diseases such as FMF, hemodialysis, or with known amyloidosis who present with a rapidly growing diffuse goiter associated with euthyroid state. Histopathologic confirmation of the diagnosis is essential. We have described two patients with extensive involvement of the thyroid gland by amyloid substance, characteristic of amyloid goiter.

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case report

A laryngeal presentation of Churg-Strauss syndrome in childhood

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Ann Saudi Med 2009; 29(2): 142-145

A 10- year-old female, known to have bronchial asthma, presented with an unusual laryngeal lesion, eventually diagnosed as Churg-Strauss syndrome (CSS). She was referred to our hospital with history of recurrent stridor. On endoscopyhe, the larynx showed signs similar to recurrent respiratory papillomatosis (RRP). CSS is a systemic disorder and is now defined as one of the ANCA (antineutrophil cytoplasmic antibodies)-associated vasculitides. CSS is a systemic disease that may involve unusual sites like the larynx. Such an unusual presenatation of CSS should be kept in mind, especially in patients with history of asthma.

Churg-Strauss syndrome (CSS) is a systemic disease characterized by asthma, blood and tissue eosinophilia, and necrotizing vasculitis with extravascular eosinophilic granulomas.[1] It is defined as one of the ANCA (antineutrophil cytoplasmic autoantibody)-associated vasculitides.[2] Despite recent interests, it is still a rare disease with a poorly understood pathogenesis. The prevalence of CSS was recently estimated at 10.7 per million adults in France.[3] Ear, Nose nose and throat involvement is a common finding, usually manifesting as allergic rhinitis and chronic rhinosinusitis with or without nasal polyposis.[4] Other rare symptoms like otitis media, facial palsy and vocal cord paralysis are also seen. In this report, we describe a unique case of CSS which presented with laryngeal mass, stridor and findings resembling recurrent respiratory papillomatosis (RRP).

CASE

A 10- year -old girl was referred to our institution, King Abdulaziz University Hospital, Riyadh, Saudi Arabia, for the management of stridor. According to the referral history, the patient was known to have bronchial asthma and used medication as needed and presented initially with difficulty in breathing at the age of 9 years. She apparently had no other medical history and was healthy prior to the first presentation. On endoscopy a growth had been seen in the larynx similar to polyposis of the larynx, and she was diagnosed as a case of RRP. That mass was excised. She again developed the same symptoms within 7 months and was operated on for another mass. She was referred for further management because of the recurrence of her symptoms.

At the time of presentation to our institute 2 months after the last surgery she had biphasic stridor, with minimal signs of respiratory distress and so was admitted for a work-up. A general examination showed that her weight was 23 kg and stature was 120cm, both below the fifth percentile, and systemic examination was unremarkable. An ear-nose-throat examination was unremarkable except that on fiberoptic endoscopy, the larynx showed a papillomatous growth involving both the true vocal cords and interarytenoid area. She had a narrow airway. Her vocal cords were mobile. Her blood work showed WBC count of 12.9×10^9/L, with an eosinophil count of 60%. The erythrocyte sedimentation rate was 54 mm/hr. Due to her recurrent attacks of bronchial asthma associated with chest infections, poor weight gain and non-resolving chest symptoms and a possible history of exposure to tuberculosis in the family, a purified protein derivative test was done and the result was negative. Serology for human papilloma virus 6 and 11 was negative. c-ANCA tested positive with a titer of 28 c-ANCA tested positive with a titer of 32 AU (more than 15 AU is considered positive, normal up to 20 AU), levels were measured using a commercially available direct PR3-ANCA ELISA kit (Euro-diagnostica, Malmö, Sweden).

Direct laryngoscopy confirmed involvement of the glottic region with a papillomatous lesion bilaterally with extension into the subglottic region mainly on the left side (Figure 1). Excision of the lesion was done using CO_2 laser and the growth was sent for histopathology , which showed multiple vessels with evidence of vasculitis and fibrin deposits in the walls (Figure 2). A number of eosinophils, plasma cells and macrophages were seen in the perivascular area. The diagnosis of CSS was made based on both histopathological and serological findings along with suggestive clinical presentation.

Within the next two months the patient had recurrence of symptoms and was again admitted with stridor. Along with stridor, she had developed a mass in the right vestibule of the nose. Flexible fiberoptic examination showed papillomatous growth involving the true vocal cord on the left side, the anterior commissure, the interarytenoid region, the subglottic region and the dorsum of the posterior third of tongue. Her vocal cords were mobile. Another surgical intervention was made to clear the airway. Excisional biopsies of the nasal mass and tongue base mass were done during the same intervention. A CT scan of the chest done postoperatively showed chronic inflammatory airway disease with a small rounded lesion in the upper lobe of the right lung. A repeat lung biopsy, which was a firm piece of tissue measuring 1×0.7×0.2 cm whose sections revealed lung tissue with parenchymal fibrosis, lymphocytic, plasma cells and eosinophilic infiltration along with fibrinoid thickening of medium-sized blood vessels and pulmonary tissue with multiple vessels showing evidence of vasculitis (Figure 3) The vessel wall showed fibrin deposits. Perivascular area showed a number of eosinophils with plasma cells and macrophages. The lung biopsy was consistent with the same pathology (CSS), as were tongue and nasal biopsies. The specimens also underwent Gomori methenamine silver and Steiner stains and was negative. Immunostains were not suggestive and culture showed no growth of micro-organisms.

At the time of the latest presentation the child was started on prednisone at a dose of 1 mg/kg/day for 6 months and this dose was tapered down over 4 month. The child was under regular follow up both by the pediatrician and our team with no further airway compromise. Her last follow-up visit was 4 years after the last intervention, when flexible fiberoptic examination of her larynx showed a clear airway. She had, however, before the last follow-up been to the emergency department from time to time for acute exacerbation

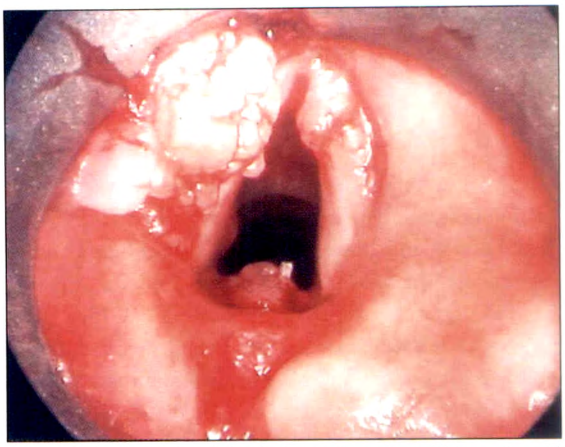

Figure 1. The lesion involving both vocal cords and interarytenoid area.

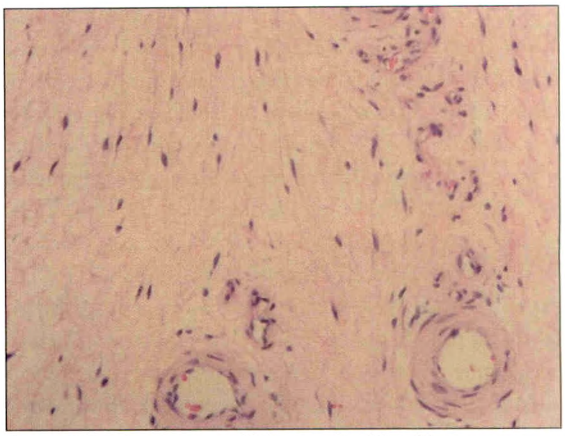

Figure 2. Section shows multiple vessels with evidence of vasculitis. The vessel walls show fibrin deposits. Perivascular area shows number of eosinophils, plasma cells and macrophages. (Hematoxylin and eosin stain original magnification ×128).

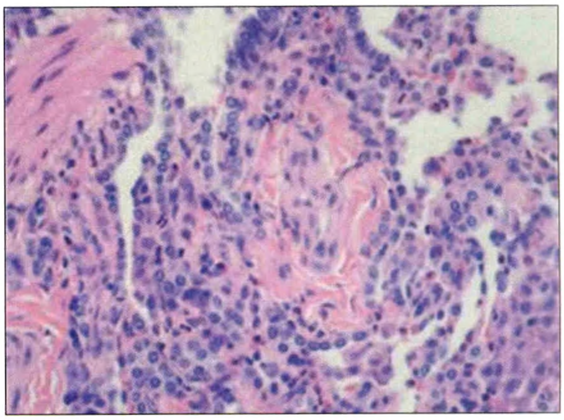

Figure 3. Section shows lung tissue with parenchymal fibrosis, lymphocytic, plasma cells and eosinophilic infiltration along with fibrinoid thickening of medium-sized blood vessels. (Hematoxylin and eosin stain original magnification ×320).

of bronchial asthma. During the course of follow-up there was no sign suggesting neurological or cardiac involvement.

DISCUSSION

CSS is a systemic disease also referred to as allergic granulomatosis, which was first described in 1951 by Jacob Churg and Lotte Strauss as a syndrome consisting of "asthma, eosinophilia, fever, and accompanying vasculitis of various organ systems".[1] Other types of systemic vasculitides are the primary vasculitis like polyarteritis nodosa and Wegener's granulomatosis and secondary vasculitis which are complications of a connective tissue disorder like rheumatoid arthritis, infection, medication or malignancy. CSS shares many of the clinical and pathological features of polyarteritis nodosa ("PAN", another type of vasculitis). Churg and Strauss discovered that the presence of granulomas as well as the abundance of eosinophils distinguished this disease from PAN. The American College of Rheumatology (ACR) has established criteria that must be fulfilled to classify a patient as having CSS.[5] These criteria were intended to distinguish CSS from other forms of vasculitis. To be classified as having CSS, a patient should have at least 4 of the 6 ACR criteria: 1) asthma, 2) eosinophilia (>10% on differential WBC count), 3) mononeuropathy, 4) transient pulmonary infiltrates on chest X-rays, 5) paranasal sinus abnormalities and 6) a biopsy containing a blood vessel with extravascular eosinophils. The presence of 4 or more of these 6 criteria yields a sensitivity of 85% and a specificity of 99.7%.[5]

Our patient clearly fulfilled five of six criteria outlined by the ACR. Interestingly, she is one of the few known cases of CSS primarily presenting with laryngeal symptoms and with laryngeal pathology. In a previous case reported by Mazzantini et al the patient's first clinical manifestation was a persistent dysphonia.[6] A videolaryngostroboscopic examination revealed paresis of the right vocal fold with a reduction in adduction together with incomplete glottal closure. Laryngeal electromyography revealed neurogenic damage of the right thyroarytenoid and crycoarytenoid muscles. In the reported case there was only neurological involvement of the larynx, but in our case the larynx was involved by a mass lesion, which is why our case is unique in presentation. To our knowledge, this is the first case reported in the literature with such laryngeal findings. There are numerous other studies of CSS presenting with gastrointestinal symptoms or with nasal symptoms, particularly allergic rhinitis and nasal polyposis,[4] and occurrence in children is infrequent.[7] Other symptoms like otitis media, facial palsy and vocal cord palsy are also seen, but rarely. Subglottic involvement of the larynx with vasculitis lesions in cases of Wegener's granulomatosis is reported, but is a rare finding.[8,9] Grans et al suggested that the presence of autoantibodies along with subglottic stenosis places such patients within the spectrum of necrotizing (granulomatous) vasculitis.[10] Other clinical studies[11] found that the clinical characteristics of patients with CCS varied according to their ANCA status: cardiomyopathy is predominant in ANCA-negative patients while necrotizing glomerulonephritis is more often observed in ANCA-positive patients. These histologically documented findings suggest the existence of different CCS subtypes, characterized by a predominance of distinct pathogenetic mechanisms.

A variety of non-invasive imaging techniques is now becoming available to investigate patients with vasculitis.[12] These include ultrasonography, MRI coupled with angiographic sequences, positron emission tomography, single photon emission computed tomography (SPECT). Their role is being evaluated and their characteristics exploited to address issues specific to each vasculitis

In conclusion, CSS is a systemic disorder and are now defined as one of the ANCA-associated vasculitites. Despite recent interest, it is still a rare disease with a poorly understood pathogenesis. This paper describes a unique case of CSS, which presented with laryngeal mass, stridor and findings resembling RRP. CSS is a systemic disease that may involve unusual sites like the larynx. Such an unusual presenatation of CSS should be kept in mind, especially in patients with history of asthma.

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Transient osteoporosis of the hip

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Ann Saudi Med 2009; 29(2): 146-148

Transient osteoporosis of the hip is an uncommon cause of hip pain, mostly affecting healthy middle-aged men and also women in the third trimester of pregnancy. We present a case of transient osteoporosis of the hip in a 33-year-old non-pregnant female patient. This case highlights the importance of considering a diagnosis of transient osteoporosis of the hip in patients who present with hip pain.

Transient osteoporosis of the hip (TOH) was first described in 1959.[1] The etiology is unknown. More than 200 cases have been reported in the literature, but the disease appears to be rare in the Asian population.[2] It is known by a variety of terms including bone marrow edema syndrome (BMED), regional migratory osteoporosis, migratory osteolysis, transient hip demineralization and transient osteoporosis. The pathophysiology is unclear. There are at least ten possible causes proposed, which include neurologic, endocrine, vascular and metabolic mechanisms.[3] In a study from Jeddah, Saudi Arabia, transient osteoporosis of the hip was diagnosed in 7 of 34 consecutive patients presenting with hip pain.[4] That study showed the importance of magnetic resonance imaging (MRI) when clinical examination is suspect for hip disorder and plain radiographs are normal or equivocal. To our knowledge, it is the only other study from Saudi Arabia discussing TOH/ BMED. TOH is self limiting and resolves symptomatically and radiologically within some months of presentation. In women TOH invariably affects the left hip.[1] Our patient presented with right hip TOH. Our case demonstrates the importance of ruling out other pathologies. TOH is a diagnosis of exclusion. Our patient was managed conservatively and made a good recovery.

CASE

We report the case of a 33-year-old Saudi female patient who was diagnosed with transient osteoporosis of the right hip. This patient presented to the Family Medicine Department at King Faisal Specialist Hospital and Research Centre, Riyadh in July 2007, with right hip pain radiating down the right leg and difficulty getting up from the sitting and lying positions. She reported straining herself after lifting heavy suitcases. The pain was relieved partially by diclofenac. She had no systemic symptoms like fever or weight loss. She remembered having pain similar to this during her pregnancy 9 years ago. She also described having left gluteal pain 2 years ago, which resolved quickly with simple analgesia. Her right leg pain persisted despite regular non-steroidal anti-inflammatory therapy. The pain was mainly experienced in the right gluteal region and radiated down the right leg to just below the knee. She reported waking at night with the pain. Her medical history included gastric banding surgery three years previously. On examination the patient was apyrexial. There was mild tenderness at L5/S1 and the right sacroiliac joint. She limped, favoring the left side. There was a slight reduction in the range of movement at the lumbar sacral spine. There was some discomfort on internal rotation of right hip but no restriction of movement. Straight leg raising was 80 degrees bilaterally with no neurological findings in the lower limbs. There was some tenderness over the right gluteal region. She found it very painful to weight bear on the right side.

Laboratory test results included the following: The erythrocyte sedimentation rate (ESR) was 21 mm/h (normal range, 0-10 mm/h). The white cell count and differential were normal. Vitamin D was <13 nmol/L (normal range, 22-116 nmol/L). Vitamin B12 was 109 pmol/L (normal range, 145-367 pmol/L). Calcium, phosphate, magnesium and alkaline phosphatase were all normal. MRI of the lumbar spine showed facet degenerative changes at L5/S1, but no focal disc herniation. As her symptoms were increasing in intensity MRI of her pelvis was arranged. This showed the following abnormalities: low signal intensity of the right femoral head and neck in T1 images, which was of high signal intensity in T2 and STIR images with some enhancement of contrast medium, particularly in the cranial medial aspect (Figure 1). These findings were suggestive of transient osteoporosis of the right hip. Mild effusion of the right hip was also noted. Incidental findings on the MRI of the pelvis included localized lynphangiomatosis and a small right ovarian cyst. In addition a small area of about 3 cm showing peripheral enhancement in the right gluteal region was noted with the comment an "infectious process is probable". The patient was referred to the orthopedic clinic urgently to rule out serious pathology. The differential diagnosis at this stage included septic arthritis, malignancy, avascular necrosis (AVN) and transient osteoporosis of the hip.

The orthopedic consultant did not feel her symptoms were due to septic arthritis as clinical and laboratory investigations did not support this diagnosis. The MRI suggested the presence of a small right gluteal abscess. The patient had received an intramuscular injection of diclofenac on this side when her symptoms first started, which was the likely reason for this appearance as there were no other signs of an abscess clinically. The MRI of the pelvis did not show signs of neoplasia or AVN. The classic appearance of AVN of the hip on magnetic resonance images is that of a local lesion of the femoral head.[6] The magnetic resonance images of our patient showed diffuse bone marrow edema with an effusion which is rarely seen in avascular necrosis of the hip. The cause of the symptoms was therefore related to TOH. The patient was initially managed with conservative measures including analgesia and strict non-weight bearing . She was prescribed calcium and vitamin D supplements. MRI of the pelvis three months after presentation showed a significant improvement, with regression of the right hip edema (Figure 2). Clinically, her pain had improved but she was advised to restrict herself to partial weight bearing only and to use crutches. One year after her initial presentation her symptoms had completely resolved.

DISCUSSION

TOH is an uncommon but important cause of hip pain. It was first described in 1959 by Curtis and Kincaid in the third trimester of pregnancy.[6] It can also affect middle-aged men, and as our case demonstrates, young non-pregnant females. It is also called BMED based on the characteristic MRI findings. Patients present with severe ill-defined unilateral hip pain without a history of trauma. Many are unable to walk without assistance. Pain is generally worse with activity. Physical examination may reveal mild limitation of hip movements with inability to bear weight even if hip pain is minimal.

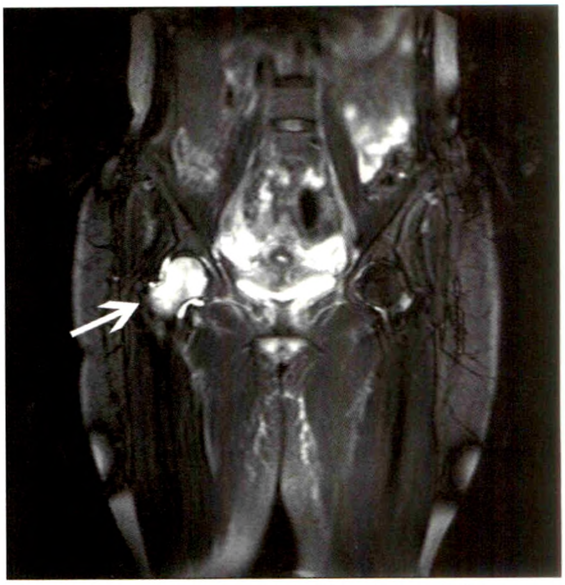

Figure 1. Initial MRI with the classical bone marrow edema picture of the right femoral head and neck.

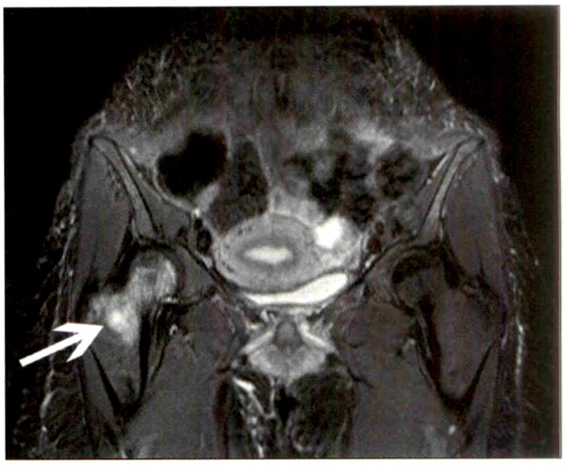

Figure 2. MRI 3 months later showing significant regression of the right hip edema.

Laboratory investigations do not help with the diagnosis, but the ESR may be elevated. Radiographic findings may lag behind clinical symptoms by 1 to 2 months.[5] In contrast, the symptoms of AVN are usually insidious in onset. Functional disability is proportionate to the level of pain. Unlike in TOH, etiological factors can be clearly identified in most patients with AVN of the hip; For example an excessive intake of alcohol and systemic administration of steroids. In our patient, an etiological factor could not be identified. In contrast to transient osteoporosis, AVN is progressive. Transient osteoporosis and AVN of the hip are two separate clinical entities that have several distinguishing clinical and radiographic features.[5]

The hallmark of TOH is its self limiting nature. The natural history of the condition is that of a symptom plateau followed by a gradual resolution of symptoms over 3 to 9 months. Migratory recurrence of symptoms occurs usually within the first 2 years after pain relief.[1] It is very important to rule out other pathologies like inflammatory arthritis of the hip, AVN, stress fracture of the femoral neck, synovial disorders and neoplasia.[7] Bone marrow edema can also be seen in hip osteoarthritis and traumatic fractures of the hip. With inflammatory arthropathies of the hip, plain radiographs show that the pattern of joint space loss is predominantly axial in contrast to the superior joint loss typical of osteoarthritis. On MRI, the typical features are of an effusion with synovitis and bone marrow edema on either side.[6]

Patients with AVN usually present with groin or hip pain. Pain may be present for several months and increases in intensity over time. Hip movements are restricted on clinical examination and symptoms tend to correlate with radiological changes. As AVN is bilateral in up to 40% of cases, both hips must be examined simultaneously.[6] The classic radiographic appearance is that of a mottled radiolucent area surrounded by an area of sclerosis. In the late stages, a radiolucent crescent sign may develop just distal to the articular surface due to subchondral collapse, before flattening of the articular surface.[2] MRI is the most sensitive and specific imaging technique for detecting transient osteoporosis and osteonecrosis as well as detecting and staging fractures and microfractures.[8] In patients with septic arthritis, MRI may depict associated marrow edema and suggest its reactive or infectious origin. For the neoplastic disorders, although plain radiographs should be the initial examination, MRI may follow for assessing extension to the surrounding soft tissues and/or associated pathologic fracture, facilitating the treatment planning.[8] MRI is therefore the investigation of choice to exclude other diagnoses. MRI in TOH shows decreased signal intensity of bone marrow on T1-images and increased signal intensity relative to the intensity of normal marrow on T2-images. Joint effusions are seen on T2-images. An absence of subchondral lesions, delayed peak enhancement of the abnormal marrow on perfusion images and sparing of the subchondral zone from marrow oedema are MRI findings highly correlated to TOH.[9] The absence of focal changes on MRI is highly suggestive of a transient lesion.[10] A greater level of awareness of this condition is needed to differentiate TOH from AVN, avoiding unnecessary surgery and ensuring appropriate treatment.[10] A careful and systematic analysis of the MR images is recommended when facing BMED of the femoral head, given the variable outcomes observed in the numerous conditions showing this syndrome.[11]

We agree with Ragab et al, who also studied BMED in Saudi Arabia, that early diagnosis and treatment of hip pain is important and MRI is the modality of choice.[4] Our findings concur with Diwanji et al on the conservative treatment of patients with TOH. Patients correctly diagnosed as having TOH usually recover well on conservative treatment.[2] Antiresorptive agents, including calcitonin and bisphosphonates, have been reported to alleviate pain and accelerate clinical and radiological recovery, although these data come from individual case reports and uncontrolled case series.[12] In the absence of clinical trials demonstrating the effectiveness of these agents, it seems reasonable to initially treat TOH conservatively, and reserve the use of antiresorptives for those with severe pain or disability, and those at highest risk of fracture.[11]

In conclusion TOH is managed with analgesia, physical therapy and protected weight bearing. This is essential to avoid stress fractures. It is important to consider TOH in the differential diagnosis of middle-aged men and young women with hip pain.

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Disseminated peritoneal *Schistosoma japonicum*: a case report and review of the pathological manifestations of the helminth

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Ann Saudi Med 2009; 29(2): 149-152

Schistosomiasis (also known as bilharzia, bilharziasis, bilharziosis or snail fever) is a human disease syndrome caused by infection from one of several species of parasitic trematodes of the genus *Schistosoma*. The three main species infecting humans are *S haematobium, S japonicum, and S mansoni. S japonicum* is most common in the far east, mostly in China and the Philippines. We present an unusual case of *S japonicum* in a 32-year-old Filipino woman who had schistosomal ova studding the peritoneal cavity and forming a mass in the right iliac fossa.

Schistosomiasis (also known as bilharzia, bilharziasis, bilharziosis or snail fever) is a human disease syndrome caused by infection from one of several species of parasitic trematodes of the genus *Schistosoma*. Approximately 200 million persons are infected with schistosomes worldwide.[1] Most human schistosomiasis is caused by *S haematobium*, *S mansoni*, or *S japonicum*. Less prevalent species such as *S mekongi* and *S intercalatum* may also cause systemic human disease. Less importantly, other schistosomes with avian or mammalian primary hosts can cause severe dermatitis in humans (e.g. swimmer's itch secondary to *Trichobilharzia ocellata*). The parasite *S japonicum* is found in the Far East, particularly China and the Philippines.[1,2] The disease manifestations caused by *S. japonicum* in humans have been extensively covered in the literature and will be reviewed in this paper. We present an unusual case of *S japonicum* where the patient had schistosomal ova studding the peritoneal cavity and forming a mass in the right iliac fossa (RIF).

CASE

A 32-year-old Filipino woman presented with a 5-day history of generalized abdominal pain and a 3-day history of nausea and vomiting. The pain settled in the RIF. She was admitted with a WBC count of 11×10^9/L and a temperature of 38.5°C. Ultrasound studies of the abdomen showed heterogeneous echogenicity of the liver (Figure 1). CT examination showed multiple calcific foci throughout the abdomen, particularly in the RIF. Prominent small bowel dilatation and fluid collection in the pouch of Douglas were also noted (Figure 2). The liver appeared surprisingly normal on the CT study. Diagnostic laparoscopy was immediately converted to an open laparotomy once a RIF mass with pus involving the appendix was seen. Dilated small bowel loops were present in the RIF and next to the spleen. The mass was dissected and released and the appendix was removed, after which the small intestinal obstruction subsided. Intraoperatively, multiple whitish yellow peritoneal nodules were noted covering the abdominal peritoneal surface and the surface of the liver. The liver, however, did not appear to be cirrhotic. On gross examination, the appendix was severely congested, measured 6×2×1 cm and showed an area of perforation at the body. The adherent omentum had focal areas of pus, and in other areas, firm yellow white nodules were present. The microscopic sections showed the appendiceal wall studded with schistosomal ova (Figure 3). Furthermore polymorphonuclear leukocytes were also seen in the wall along with areas of suppurative inflammation and necrosis. Sections from the adherent omental mass also showed suppurative inflammation and multiple foci of shistosomal ova. The ova were oval to round in shape and showed outpouchings highly indicative of *S japonicum* species

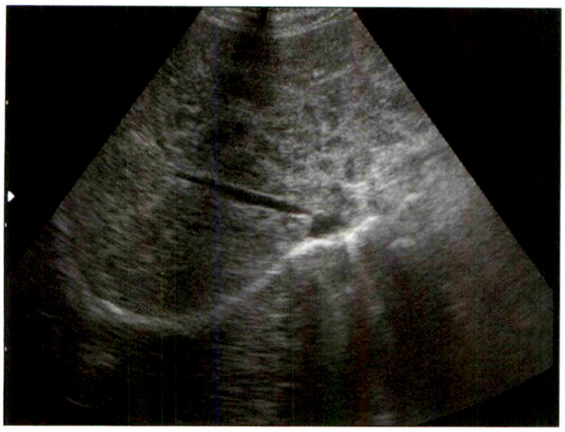

Figure 1. Ultrasound of the liver shows heterogenous echogenicity.

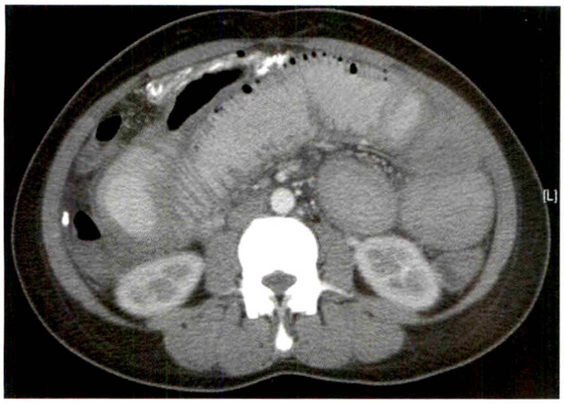

Figure 2. CT scan shows multiple dilated small bowel loops with multiple calcific peritoneal deposits.

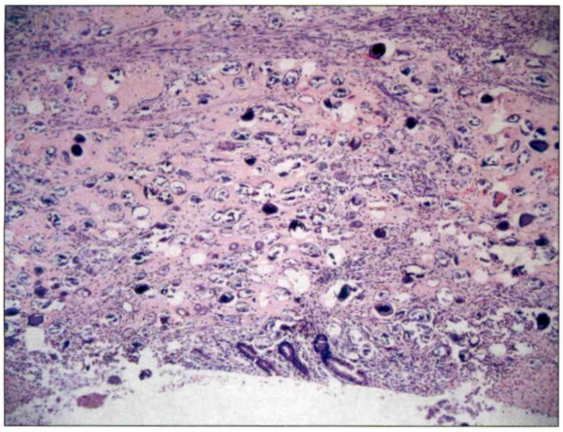

Figure 3. Appendiceal wall studded with schistosomal ova (hematoxylin and eosin stain ×200).

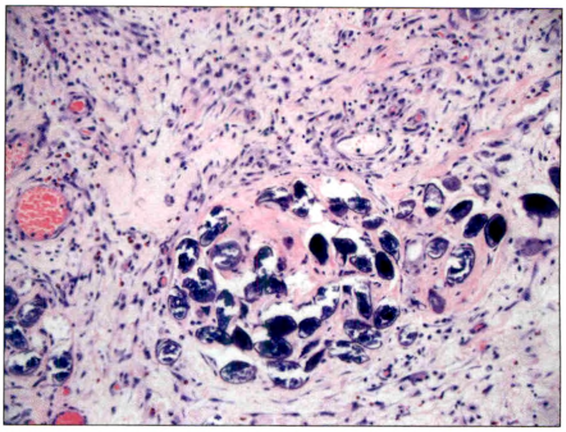

Figure 4. *Schistosoma Japonicum* ova with characteristic lateral outpouchings (hematoxylin and eosin stain ×200).

(Figure 4). No granulomatous response was present in the sections examined. Stains for bacterial, fungal and acid fast organisms were all negative. The histopathologic diagnosis was acute suppurative appendicitis and peritonitis with disseminated schistosomal ova involving the appendix and omentum.

DISCUSSION

From a clinical perspective *S japonicum* usually causes an acute serum sickness also called 'Katayama' fever,[3] which is associated with the onset of the female parasite laying eggs (approximately 5 weeks after infection) and granuloma formation around eggs trapped in the liver and intestinal wall. It manifests with hepatosplenomegaly and leucocytosis with eosinophilia. This phase of the infection is often asymptomatic, but when symptoms do occur they include fever, nausea, headache, an irritating cough and, in extreme cases, diarrhea accompanied with blood, mucus and necrotic material. These symptoms, if present, last from a few weeks, to several months and are not as commonly associated with *S hematobium* or *S mansoni* infections compared with those of *S japonicum*. The chronic phase of infection, however, is the more important part of the infection.[3] From a pathological perspective, common morphological manifestations of the chronic phase are intestinal and hepatic schistosomiasis. Both manifest a number of years after infection. A large autopsy study involving 349 cases showed that the dominant pathology is evident in the liver.[4] The pathogenic reaction is a cellular, granulomatous inflammation around eggs trapped in the tissues, with subsequent fibrosis. Specific liver pathology was destruction of limiting plates, reparative hepatic lesions such as regeneration of the collapsed parenchyma, newly formed limiting plates and subsequent narrowing and disappearance of fibrous septa. In more chronic lesions, fibrosis and cirrhosis are seen. Complications of liver cirrhosis and hepatocellular carcinoma related to viral hepatitis B and/or C were also increased. Clonorchiasis was also consistently found.[4] All areas of both the small and large intestine may be involved, with the large intestine showing the most severe lesions, whereas severe pathology in the small intestine is only rarely observed, even though a large number of eggs may be deposited there.[5] The theory is that the adult worms have a predilection for inhabiting the branches of the inferior mesenteric vein and superior haemorrhoidal vein and their eggs are deposited in much higher density in the large intestine, especially in the rectum, sigmoid and descending colon, than in the small intestine.[5] Gastrointestinal findings may include polyp formation. The friable vascular nature of these inflammatory polyps may lead to lower gastrointestinal bleeding.[6] Large polyps, or bilharziomas, may cause intestinal obstruction, intussusception, or be confused with a malignancy.[7] Colonic polyps are of higher prevalence in Egypt for reasons that are not clear.[8] Other cited gastrointestinal findings may include strictures, fistulae and bowel perforation.[7,9] *S japonicum* eggs may also be deposited in the appendix and may manifest as appendicitis. Schistosomal appendicitis acquired in a traveler has been described.[10]

Liver-related and gastrointestinal complications can be prevented with early recognition and therapy of schistosomiasis. In a radiologic study of 12 patients that underwent CT of the abdomen to detect what proved to be *S japonicum* by pathologic examination, the CT demonstrated curvilinear or nodular calcification in the colon in 11 patients, in the appendix in 2, and in the distal ileum in 1 patient. Pathologic examination of the specimens showed calcified eggs of *S japonicum* deposited more extensively in the submucosa and subserosa than in the muscularis propria, which led to the curvilinear appearance.[6] The pathology in the liver is similar to that seen in the intestine, with a cellular, granulomatous inflammation around eggs trapped in the liver, leading to fibrosis and hepatosplenic disease and subsequent cirrhosis in chronic disease. Studies on the effect of *S japonicum* and the liver have been recorded since the early 1970s from endemic areas.

Kurniawan et al studied 52 *S japonicum*-infected patients from an endemic area in Indonesia.[11] All of these patients exhibited signs and symptoms of chronic hepato-splenic schistosomiasis. None of the patients showed evidence of liver cirrhosis on histopathological examination. However, varying degrees of portal fibrosis were exhibited and the authors concluded that liver biopsy has proved to be a valuable method of diagnosis in this particular type of infection. *S japonicum* resides in the mesenteric veins which drain to the liver, and therefore causes liver fibrosis after depositing in that organ.[12] A study of the ultrasound and CT scan findings of patients with biopsy-proven hepatic *S japonicum* revealed characteristic findings.[13] They observed a "network pattern of calcification" on ultrasound and a "turtle-back" pattern on contrast CT scan. Laparoscopic findings of nine patients with chronic *S japonicum* were analyzed and compared with histological findings from the same patients.[14] In all nine patients laparoscopy revealed yellowish, small speckles clustered over the liver surface, which were later found to be the subcapsular calcified ova of *S japonicum*. While the liver surface was almost smooth in mild schistosomiasis, multiple whitish markings and irregular, relatively wide, groove-like septums were seen in more advanced cases. In severe schistosomiasis, block-like formations of variable size, separated by groove-like depressions, made the liver surface appear like a tortoise shell on the CT scan. Other organs may rarely contain granulomas around eggs, like the breast[15] and fallopian tube.[16]

What is unusual and novel about our case from a morphologic perspective is that there has not been a reported case in the English language literature of *S japonicum* disseminating and covering the peritoneum in this. The patient was lost to follow-up and no colonoscopy was done to rule out any colonic pathology which may have been present in the patient. Similarly, the liver might have been involved with *S japonicum* ova, as suspicious nodular lesions were seen studding the surface of the liver intraoperatively, but no liver biopsy was performed. The liver enzymes were normal in the patient and no overt liver cirrhosis was present. The other unusual feature was the lack of a granulomatous reaction in the tissue examined in our laboratory.

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A 3-year-old boy with a depressed, whitish lesion on the left buttock

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Ann Saudi Med 2009; 29(2): 153

A 3-year-old Saudi boy with severe atopic dermatitis presented with a depressed white area on the left buttock. Three weeks previously, the parents noticed this insidious onset, asymptomatic, whitish depression in the left gluteal area. His medical history was not significant except for a chronic history of severe atopic dermatitis. On physical examination, there was a well-defined, round hypopigmented, atrophic plaque on the left buttock (Figure 1). There were no other areas of atrophy with normal fat distribution elsewhere on the body.

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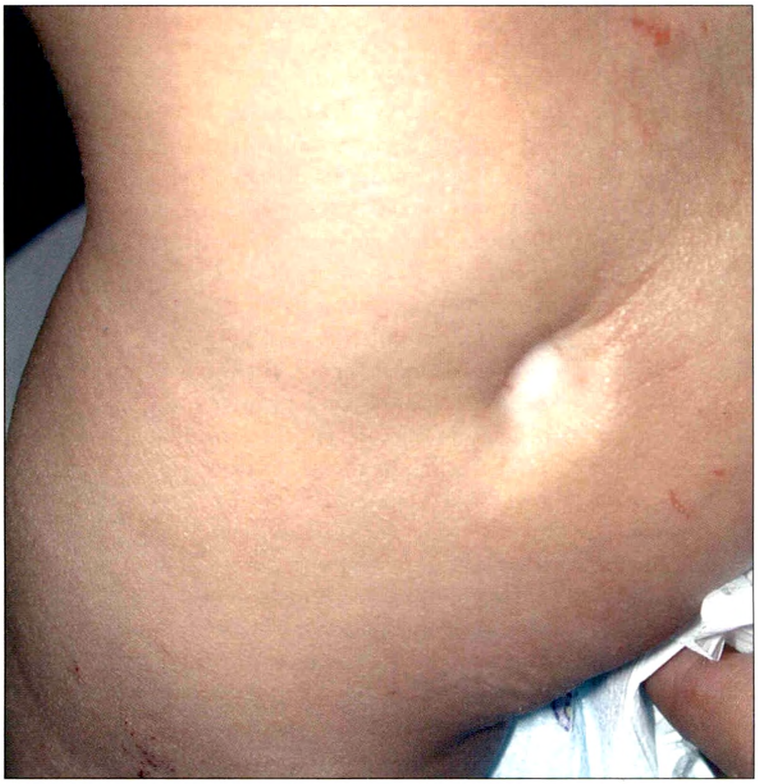

Figure 1. A depressed, whitish lesion on the buttocks.

Difficulties in diagnosing tuberculosis in pregnancy

To the Editor: Diagnosing tuberculosis (TB) in pregnancy can be difficult because of the vague, non-specific nature of the symptoms. Fatigue, shortness of breath, sweating and tired, all characteristic of TB, can also be due to pregnancy. Most physicians are reluctant to order a chest x-ray for fear of harming the fetus. This case illustrates the problems in early recognition and management of TB in pregnancy.

An 18-week pregnant woman who had a low-grade fever for 3 months underwent an extensive and unnecessary work up for pyrexia of unknown etiology. All tests were normal including a bone marrow biopsy. Due to concerns over harming the fetus, a chest x-ray was not performed. MRI of the chest and abdomen showed a miliary pattern. The diagnosis was tuberculosis (TB). A sputum culture was positive for acid-fast bacilli and sensitive to first-line anti-TB therapy. A chest x-ray requested 2 weeks after admission showed the miliary shadow. A PPD skin test was negative. The patient received anti-TB therapy for 9 months without complications. She had a baby girl who was healthy.

Treatment of TB in pregnancy is multidisciplinary, requiring input from all physicians involved in the care of the mother and fetus. Between 20% and 67% of pregnant patients presenting with pulmonary TB are unaware of their disease and have no significant symptoms.[1] Available information suggests that pregnancy has little, if any, effect on the clinical course of TB.[2] Screening for TB in pregnancy is not required because of the reluctance to do a chest x-ray on a pregnant women. A review of TB diagnoses in Rhode Island, USA from 1987 to 1991 found that pregnant women with TB were most likely to be identified through routine screening and to be asymptomatic.[1]

If the chest x-ray is necessary, suitable shielding will limit fetal radiation exposure to less than 0.3 mrads and should not harm the fetus.[3] The perception of teratogenic risk is higher than the actual risk.[4] MRI uses electromagnetic radio waves, rather than ionizing radiation, to generate detailed computer images. There are no reported harmful effects from MRI on the pregnant woman or fetus.[5] However, MRI is not recommended in the first trimester since safety information during organogenesis is limited. A TB skin test using purified protein derivative (PPD) is safe and accurate during pregnancy and is recommended for women who have TB symptoms or are at high risk for TB. It is as reliable as in non-pregnant women.[6,7] No evidence suggests that TB affects or complicates either the course of pregnancy or delivery; women with and without TB have similar rates of normal, spontaneous deliveries.[9] Combination anti-TB therapy in pregnancy is safe and effective. Most experts consider the drugs of choice to be rifampin, combined with isoniazid and ethambutol.[10] All these drugs cross the placenta and reach low concentrations in human fetal fluids and tissues, but there are no reports linking the use of these drugs with congenital anomalies. The following anti-TB drugs are contraindicated in pregnant women: streptomycin, kanamycin, amikacin, capreomycin and the fluoroquinolones. Women on second-line agents for multi-drug resistant TB need to be assessed on an individual basis regarding their risks. Women who become pregnant on anti-TB therapy can be reassured that there is no increased risk to their baby, and they should complete their treatment course.[8-10]

Breastfeeding should not be discouraged for women being treated with the first-line anti-TB drugs because the concentrations of these drugs in breast milk are too small to produce toxicity in the nursing newborn.[8]

Congenital TB in neonates has morbidity and mortality approaching 50%.[11] About 200 cases have been reported in the English literature.[12,13] The child can be infected in the uterus if the mother has had miliary TB, TB of the placenta or uterus, or has advanced HIV.

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Aphalangia possibly linked to unintended use of finasteride during early pregnancy

To the Editor: Finasteride (Proscar) is a 5-alpha reductase inhibitor used for treatment of benign prostatic hyperplasia.[1] Finasteride is not FDA-approved for use in women,[2] but in practice is prescribed with warnings about becoming pregnant. A teratogenic effect on the human fetus has not been reported, but animal studies show external genital abnormalities in male fetuses exposed to the 5-alpha reductase inhibitor in utero so the drug is classified in FDA pregnancy category X (studies in animals or pregnant women have demonstrated positive evidence of fetal abnormalities) and is contraindicated in women who are or may become pregnant.[3,4] We report a case of unintended use of finasteride during early pregnancy. The pregnancy ended with the normal delivery of a baby girl with unilateral hand and toe deformities.

A 41-year-old woman, gravida7 para6, was urgently referred to the Maternal-Fetal Medicine (MFM) clinic at King Fahad Medical City. She was seeing a dermatologist due to male pattern alopecia after her last delivery. Finasteride 1 mg was prescribed, and she was warned against pregnancy. However, she did not use contraception because she was breastfeeding and thought she would not become pregnant. Unfortunately, pregnancy was confirmed after a history of 6 weeks of amenorrhea. Finasteride was stopped immediately. She had six previous healthy children and was not known to have any chronic medical illnesses. The family history was unremarkable for congenital anomalies or genetic diseases. She used no medication other than finasteride and there was no history of radiation exposure.

She was counseled about its general and specific (abnormalities of external male genitalia) teratogenic effects of finasteride during the current pregnancy. Ultrasound examination was performed at 12 weeks of gestation (for nuchal translucency, nasal bone and ductus venosus), and was unremarkable. A detailed anatomy ultrasound scan at 18 and 26 weeks of gestation found no anomalies. Because the fetus was a female, the mother was reassured. For the rest of her antenatal care, the pregnancy was uneventful. At term, she delivered a baby girl with a normal birth weight of 3850 g (appropriate for gestational age), a height of 53 cm (at 50th percentile), a head circumference of 34 cm (above 10th percentile), a chest circumference of 33 cm, and abdominal girth of 33 cm. The baby was found to have deformities in the right hand in the form of a small hand with short fingers and absent phalangial bones in all five fingers (aphalangia) (Figure 1), and in the left foot in the form of short second and third toes with absent distal phalanges. Two cafe au lait spots were seen also on the back. No other abnormalities could be

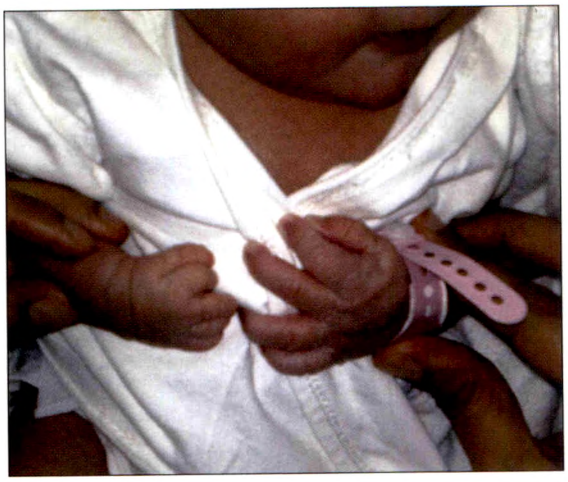

Figure 1. Note the small right hand with short fingers.

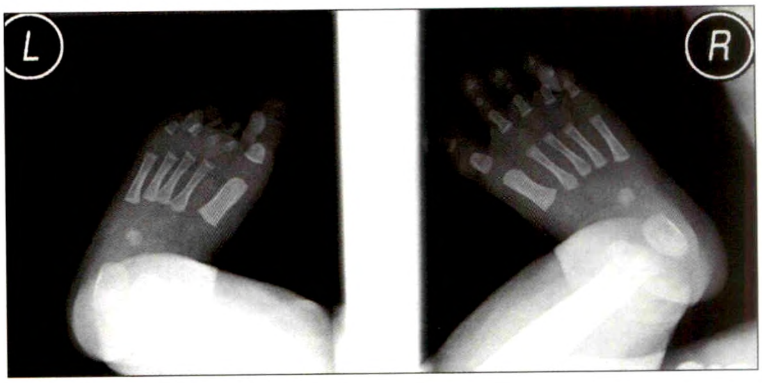

Figure 2. X-ray of both feet. Note the short toes on the left foot with absent phalanges in the second and third toes.

identified. X-ray examinations of upper and lower limbs confirmed the clinical findings. Abdominal ultrasound examination was unremarkable (Figure 2).

Limb formation begins at the fourth week of embryonic life. The limb primordium bulges from the body wall consisting from mesoderm covered by a layer of ectoderm. An apical ectodermal ridge (AER) is a thickened ectoderm located at the apex of the limb. Animal studies have confirmed that removal of the AER results in the arrest of limb development. The degree of deformity depends on the time of insult; the more mature the limb bud, the more the skeletal element forms after AER removal.[5] In the current case, x-ray of both hands showed absent phalangial bones in the right with normal phalanges in the left, and normal metacarpal bones in both. The carpal bones are normally not noticeable in the x-ray at this age. It is known that ossification of the phalanges takes place antenatally, while the carpal bones ossify postnatally.[6] Limb anomalies can usually be diagnosed by antenatal ultrasound scan; nevertheless, we missed the diagnosis antenatally, mainly due to lack of suspicion for such potential deformities with the use of finasteride in pregnancy. The appearance of one normal hand could be misleading and result in missing the other abnormal hand. The toe deformities were minor and would have been difficult to discern by antenatal ultrasound examination. The finding of a female fetus was a reassuring sign. To our knowledge, this is the first case report of finasteride use during pregnancy in a human. It is not clear if these deformities are related to finasteride use in pregnancy, but it is worthwhile to document a possible association and focus attention on the possibility of limb deformities in such cases.

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Transverse myelitis as a presenting feature of late onset systemic lupus erythematosus

To the Editor: Late-onset systemic lupus erythematosus (SLE) is the type of SLE whose manifestations reportedly begin after the age of 50[1-3] or 65 years.[4] The prevalence of transverse myelitis (TM) in SLE patients is 1% to 2%.[5] It can occur as the initial manifestation of SLE in up to 39% of patients.[5] TM as a presenting feature of late-onset SLE is rare. Only a few cases have been reported.[5-7] We report on a previously healthy 65-year-old female patient who presented to our hospital with a month-long history of progressive weakness, numbness of the lower limbs and unsteady gait that was associated with loss of bowel and bladder control. She also reported an intermittent history of fever but no weight loss, or night sweats, headache, vomiting or seizure activity. She was conscious, alert and oriented to place, person and time. Her temperature was 38.0°C, heart rate 123 beats/minute, blood pressure 155/80 mm Hg and respiratory rate 18 per minute with 98% oxygen saturation. Examination of the cranial nerves was unremarkable. Motor examination showed hypotonia in the lower limbs with a power of 0/5, absent reflexes and downgoing planter responses bilaterally. There was loss of all sensation up to the nipples at the level of T4. Investigations at presentation showed neutrophilic leukocytosis with lymphopenia, an elevated PTT of 45 seconds[1] and an erythrocyte sedimentation rate of 5 seconds with normal renal and hepatic profiles. Cerebrospinal fluid (CSF) analysis showed pleocytosis; white blood cells (WBC) of 3.71×10^9/L with 75% lymphocytes, glucose of 5.5 mmol/L, protein of 1419 mg/L and negative cultures for all bacteria and viruses including acid fast bacilli. PCR for acid fast bacilli was negative as well. Urine culture was positive for *E. coli*. MRI of the spine and brain with T1-and T2-weighted sagittal and axial images including a magnetic resonance angiogram showed normal brain parenchyma and diffuse hyperintensity within the cord at the level of thoracic spine T1 extending up to T10. The diagnosis of idiopathic TM was made. She was treated with pulse therapy with IV methylprednisolone (1 gram) for 5 days and intravenous ceftriaxone. Her condition improved significantly with power increased from 0/5 to 3/5 in the lower limbs. Two weeks later, despite taking an oral steroid, power over her lower limbs was 0/5 again.

The repeat MRI showed multifocal areas of significant hyperintensity within the thoracic spine with multifocal enhancement in the posterior aspect of the cord post gadolinium (Figure 1). Anti-tuberculosis medications were initiated and discontinued when acid fast bacilli were not isolated by cultures and PCR technique. Rheumatological assessment after approximately 1 month of hospital admission revealed a positive antinuclear antibody (ANA) test with a titer of 1:320. The anti-ds DNA antibodies were repeatedly positive at 32.9 IU/mL (normal less than 10 IU/mL). Lupus anticoagulant was positive as well. She was diagnosed with TM as a presenting manifestation of SLE with antiphospholipid antibodies. Another pulse therapy with IV methylprednisolone (1 gram) for 5 days was started. The patient preferred not to receive any additional therapeutic interventions. Her weakness improved significantly with a power of almost 5/5 over limb girdle muscles 8 months after discharge. The repeat MRI demonstrated some improvement in previously present hyperintensity within the upper thoracic cord.

The management of TM continues to represent a major therapeutic challenge for clinicians in daily practice. The ideal drugs, doses, and the length of treatment are not yet well defined. In older studies, most patients were treated with IV corticosteroids alone, whereas more recently some centers prefer a more aggressive approach with IV methylprednisolone pulse therapy plus IV cyclophosphamide. There were no clear differences between these drugs in five cases of TM when both were studied against each other after induction therapy with methylprednisolone.[8] However, several studies reported good to fair functional outcomes with combined treatment.[6] The majority of TM cases reported in the literature were positive for antiphospholipid antibodies: 73% in one series[6] and 55% to 64% in another.[5] One of the strongest risk factors for the development of significant neuropsychiatric damage was the presence of antiphospholipid antibodies.[9] This has resulted in the introduction of anticoagulant therapy in the management of TM patients with positive antiphospholipid antibodies, but this practice remains controversial. Plasmapheresis has been used to complement this treatment regimen,[5,10,11] but it is still unclear if it has any additional therapeutic benefit. There are recent reports on the successful use of anti-CD20 in patients with TM.[12,13] The patient described in this letter had significant improvement with the use of steroids alone. TM in the elderly might be controlled with the use of a large dose of steroid.

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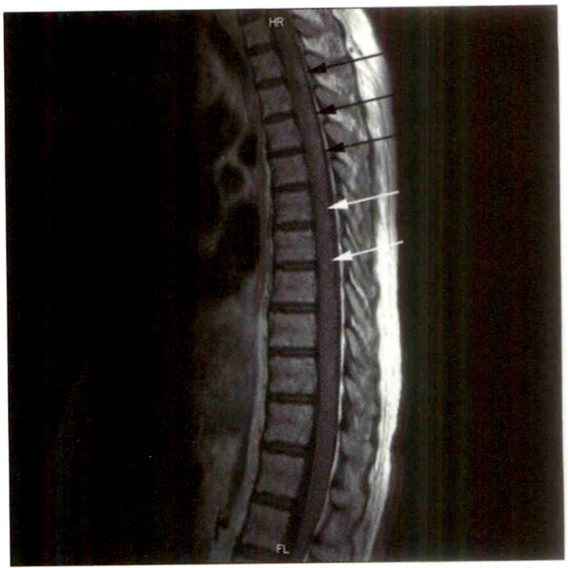

Figure 1. MRI of the thoracic spine (sagittal view T1-weighted post-gadolinium image) showing some multifocal areas of enhancement within the cord that predominantly involve the posterior aspect of the cord (black arrows).There are also extensive focal small enhancing lesions (white arrows).

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Bilateral brucellar breast abscess in a 48-year-old woman

To the Editor: Brucellosis is a zoonotic infection transmitted from animals to humans by ingestion of infected food products, direct contact with an infected animal, or inhalation of aerosols.[1] The disease remains endemic in many countries, mainly in the Mediterranean basin, the Middle East, India, Mexico, Central and South America and, currently, central and southwest Asia. Soft tissue involvement is an uncommon occurrence of the disease. Breast involvement in animals is common, whereas in humans it is an extremely rare manifestation.[2-5] We report a case of bilateral brucellar breast abscess, which was successfully treated through abscess drainage and antibiotic therapy.

A 48-year-old woman was admitted to our department with pain, swelling, erythema, and an odorless nipple discharge in both breasts for 10 days. She was involved in stockbreeding on a farm and was suspected of having a history of consumption of unpasteurized cheese. She had also been suffering from night sweats for the previous 2 years. Physical examination revealed a 5×3 cm, indurated, erythematous, and painful mass in the upper left quadrant of the breast on the left side and 3×3 cm periareolar painful mass in the right breast. Bilateral abscess formation with cystic and solid components were detected through ultrasonographic examination of both breasts. Needle puncture of the lesions revealed an obvious purulent material. Bilateral surgical drainage was performed. Oral antibiotic therapy with cefuroxime axetil was began immediately due to a suspected pyogenic abscess. Despite daily wound dressing changes of the abscess cavities and scheduled antibiotic therapy, the patient did not improve.

Approximately 2 weeks after primary abscess drainage, bacterial culture of the purulent material revealed *Brucella* species. Following the positive culture for *Brucella*, the Wright and Rose-Bengal tests were also found to be positive, which confirmed the diagnosis of human brucellosis and bilateral brucellar breast abscess. After replacing the ongoing antibiotic therapy with combined regimen of oral doxycycline (200 mg/day) and rifampin (600 mg/day), dramatic regression of both of the abscesses and rapid improvement in clinical symptoms were observed, which also confirmed the diagnosis of human brucellosis. The 6 month follow-up was uneventful.

Brucellar infection of the human breast is extremely rare. Clinical symptoms of brucellosis are nonspesifics and include fever, malaise, sweats, arthralgias, lower back pain, and headache. Based on the series of Andriopoulos et al, the prevalence of human brucellosis as a breast abscess is only 0.7%.[6] Our case presented with bilateral breast abscesses first though to be pyogenic. Unfortunately, bilateral surgical abscess drainage followed by broad-spectrum oral antibiotic therapy did not heal the abscesses. The delay in the definitive diagnosis of the causative agent of the breast abscess was the most likely reason for failure of treatment. The clinical management of brucellosis is of particular concern because of high initial treatment failure and relapse rates.[7] Two weeks after initial treatment we were able to replace our initial treatment regimen with appropriate combined antibiotic therapy based on the definitive isolation and positive culture for *Brucella* species as the causative agent in our patient. Although the breast abscess is a very rare complication of systemic brucellosis, the physician should be aware of this unusual manifestation of human brucellosis. We concluded that repeated cultures from purulent material in an unhealing breast abscess, despite the broad-spectrum antibiotic therapy and surgical drainage, may eventually show underlying systemic brucellosis, especially in endemic areas of the world.

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RE: Snake venom preparation for drug-resistant human immunodeficiency virus

To the Editor: Recently the usefulness of snake venom preparation in the treatment of drug-resistant human immunodeficiency virus was demonstrated in clinical practice for the first time by Alrajhi and Almohaizeie.[1] This represents an emerging concept in the era of anti-retroviral therapy (ART). The authors have reported that snake venom might have enhanced the activity of ART or independently through some of its components. With reference to mechanisms of action, other components of snake venom such as the sequence homology between venom and HIV-1 gp 120[2] and protease[3] might also have contributed to the enhanced activity of ART at different levels.

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CONSORT (Consolidated Standards of Reporting Trials), is part of a broader push to produce reporting guidelines (RGs) for many different types of research. The main product of CONSORT is the CONSORT Statement, which is an evidence-based, minimum set of recommendations for reporting RCTs. It offers a standard way for authors to prepare reports of trial findings, facilitating their complete and transparent reporting, and aiding their critical appraisal and interpretation. The CONSORT Statement comprises a 22-item checklist and a flow diagram, along with some brief descriptive text.

ASSERT

The ASSERT **(A Standard for the Scientific and Ethical Review of Trials)** initiative is a proposed standard for the review and monitoring of randomized clinical trials by research ethics committees. Among other items, its checklist incorporates certain elements of CONSORT, to ensure fulfillment of the requirements for scientific validity in the ethical conduct of clinical research.

MOOSE

The MOOSE **(Meta-analysis of Observational Studies in Epidemiology)** paper reports the outcome of a 1997 workshop to examine the reporting of meta-analyses of observational studies. It makes recommendations to aid authors, editors, reviewers and readers of observational research.

QUOROM

The QUOROM **(Quality Of Reporting Of Meta-analyses)** conference resulted in the creation of the QUOROM Statement, which consists of a checklist and flow diagram.

STARD

The STARD **(Standards for Reporting of Diagnostic Accuracy)** initiative aims to improve the accuracy and completeness of reporting of studies of diagnostic accuracy in order to allow readers to assess the potential for bias in a study and to evaluate the generalisability of its results.

King Faisal Specialist Hospital & Research Centre

Symposium:

The Health Consequences od Global Warming
06-07 October 2009
17-18 Shawwal 1430

Workshops:

Vascular Access in Dialysis Patient Workshop
04-05 April 2009
08-09 Rabia Al Thani 1430

Courses:

7th Pediatric Intensive Review Course
26 September-01 October 2009
07-12 Shawwal 1430

Academic & Training Affairs
CME Section (MBC 36)
King Faisal Specialist Hospital & Research Centre
P.O. Box 3354, Riyadh 11211
Saudi Arabia
T: +966-1-442 7238,
F: +966-1-442 4153/442-7237
web_symposia@kfshrc.edu.sa

World Health Organization
Regional Office for the Eastern Mediterranean

Directory of Health, Medical Conferences and Professional Meetings in the Region

http://www.emro.who.int/conf/

Objectives

To develop and maintain a directory of conferences and meetings organized by government institutions, academic bodies and other non-profit professional organizations in the Region.

The directory will:
- Serve as a vehicle to distribute information on these events to health care professionals and academicians;
- Enhance networking and collaboration between institutions;
- Record professional events for the future reference and archiving of conference proceedings as much as possible;
- Alert health care professionals and academicians to the new conferences related to their speciality.

Section of Colorectal Surgery Fellowship Training Program

A two-year clinical fellowship program that aims to provide the candidate with the basic science, clinical and operative skills to manage patients with colorectal diseases competently. The operative load of the Section is 300 operations annually. The majority of such operations are complex colorectal conditions such as colorectal cancer, fecal incontinence, complex anal fistulae and complicated inflammatory bowel disease conditions. The fellowship provides training into diagnostic and therapeutic colonoscopy such as insertion of colonic stents for bowel obstruction. Moreover, training into endoanal and endorectal ultrasound for the assessment of anal sphincters and staging of rectal cancer will be provided, respectively. An important aspect of the program is training into anorectal physiology testing and the interpretation of such complex data. During training, the fellow will be exposed to Enterostomal therapy and all aspects of stoma care. The Section holds an annual colorectal surgery symposium and the fellow is expected to be an active member in this activity, which includes presentation and publication of medical literature in the area of colorectal surgery. Laparoscopic colorectal surgery will be an integral part of training along with standard open surgery. The Section has a well-established curriculum of teaching activities such as morbidity and mortality meetings, radiology rounds and GI clubs. The fellow is expected to participate actively in these educational activities.

For interested applicants, please contact:
Academic & Training Affairs
T: 442-7214/5
ata@kfshrc.edu.sa

The Palliative Medicine Fellowship Program

King Faisal Specialist Hospital & Research Centre, Riyadh
One-Year Fellowship Program

Applicants:
1. Must be Saudi nationals.
2. Must be Saudi Board (or equivalent)
certified in one of the following specialties:
Family Medicine, Internal Medicine, Anesthesiology, General Surgery &
Boards in other specialites may be considered on indiviudal basis.

For information, please contact: Academic & Training Affairs; King Faisal Specialist Hospital & Research Centre; P.O. Box 3354, MBC 36; Riyadh 11211, Kingdom of Saudi Arabia. T: +966-1-464 7272 ext. 31833; F: +966-1-442 7237

announcements

Hepatobiliary-Pancreatic Surgery Fellowship Program

KFSH&RC-Riyadh, Saudi Arabia

Hepatobiliary-Pancreatic Surgery Fellowship Program is a compherehensive structured educational program designed to graduate independent surgeons with high standards of skills, broad knowledge and proficient in clinical decisions. The fellow will attain proficiency in endoscopic procedures, be able to interpret radiological investigations exam as well a take care of basic and complex hepatobiliary-pancreatic surgical procedures.

The Department of Liver Transplantation and Hepatobiliary-Pancreatic Surgery at King Faisal Specialist Hospital & Research Center offers:

- Four qualified hepatobiliary and transplant consultant surgeons with good experience in teaching and commitment to provide academic teaching and training.
- A very good facility in interventinal radiology.
- Equipped Operating rooms and intensive care facility.
- Outstanding internet access for library service for research resources as well as outstanding research facility and database available for research users.

The Fellowship Program is for two years and there are two positions available for application. Qualified candidates can direct their query to:

Academic & Training Affairs
KFSH&RC-Riyadh (MBC 36)
P.O. Box 3354, Riyadh 11211, Saudi Arabia
T: +966-1-442-7215/442-7214
F: +966-1-442-7237
ata@kfshrc.edu.sa

12th World Congress on Public Health

Making a Difference in Global Public Health:
Education, Research and Practice
27 April-01 May 2009 Istanbul, Turkey
World Federation of Public Health Associations and the Turkish Public Health Association
www.worldpublichealth2009.org

The abstracts should also showcase innovations, practices, tools and transferable lessons from across the globe that will help us make a decided difference in global public health. We invite you to submit abstracts in the following general topics:

- Education in Public Health for 21st Century
- Global Public Health Workforce
- Public Health & Health Services Research & Technology
- Global Governance
- Health and Development
- Comparative Analysis of Health Systems
- Strengthening Global Public Health Systems
- Financing Global Public Health
- Environmental Safety & Stewardship
- Health, Geopolitics, & Public Diplomacy
- Public Health, Political Will, & the Public Good

3rd International Saudi Orthopaedic Association Conference

18-22 January 2010

Department of Orthopaedic Surgery, King Faisal University will be organizing the 3rd International Saudi Orthopaedic Association Conference in Alkhobar from 18th to 22nd of January 2010.

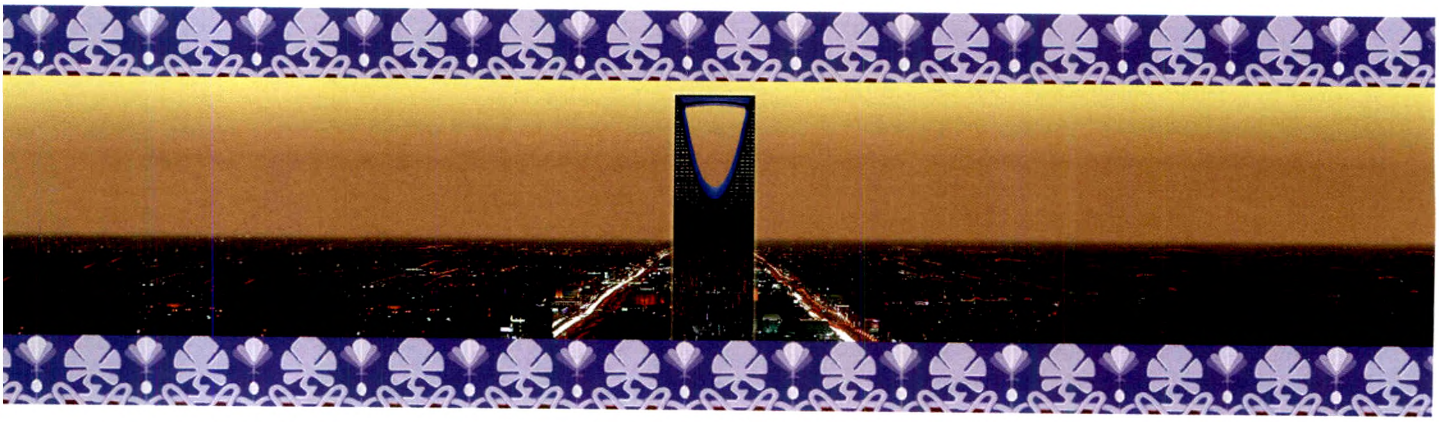
Abstracts can be submitted by e-mail:
SOAC2010@gmail.com or by
Fax: 03-8966735.

Deadline for Abstracts Friday 5th June 2009.

Prof Ibrahim Al-Habdan
Chairman Organizing Committee,
3rd Saudi Orthopaedic Association Meeting
AlKhobar 18th-22 nd Jan 2010

مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة

CANCER CYTOGENETICS CONFERENCE 2009



2-3 Jumada Al Thani 1430
26-27 May 2009

Prince Salman Auditorium

King Faisal Specialist Hospital and Research Centre
Riyadh, Kingdom of Saudi Arabia

International Speakers

- **Claudia Baldus**, Berlin, Germany
  Charité, University Hospital
- **Georgia Bardi**, Athens, Greece
  Greek General Secretary of Research and Technology
- **Paola Dal Cin**, Boston, USA
  Harvard Medical School
- **Sverre Heim**, Oslo, Norway
  Norwegian Radium Hospital / Rikshospitalet University Hospital
- **Ruben Mesa**, Rochester, USA
  Mayo Clinic
- **Anthony Moorman**, London, UK
  Northern Institute for Cancer Research, Newcastle University
- **Cynthia Morton**, Boston, USA
  Harvard Medical School
- **Daniel Van Dyke**, Rochester, USA
  Mayo Clinic

Organizer

Department of Pathology &
Laboratory Medicine, Section Cytogenetics

Contacts

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Conference Secretary
Tel +966-1-442-7224
Fax +966-1-442-4280
Email garcia@kfshrc.edu.sa

Claudia Walter
Chairperson Organizing Committee
Tel +966-1-442-4228
Fax +966-1-442-4889
Email cwalter@kfshrc.edu.sa

Registration

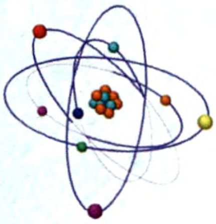
www.kfshrc.edu.sa/symposia
www. cancer-cytogenetics-2009-kfshrc.com

ACCREDITED BY SAUDI COMMISSION FOR HEALTH SPECIALTIES

ACCREDITED BY AMERICAN ACADEMY OF CONTINUING MEDICAL EDUCATION

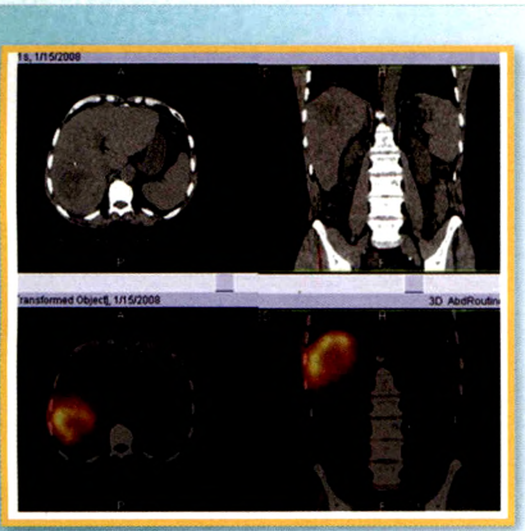
DESIGNED BY PHOTOGRAPHICS

ADVANCES *in* MANAGEMENT OF
THYROID CANCER
NEUROENDOCRINE TUMORS & LYMPHOMAS
(THE ROLE OF RADIONUCLIDE THERAPY)



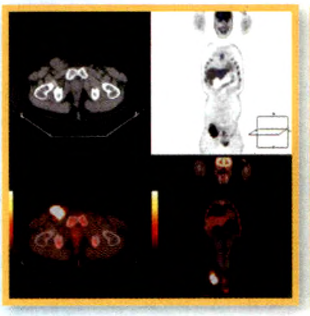
02-04 MAY 2009
(07-09 Jumada AlAwal 1430)
Postgraduate Centre
Auditorium

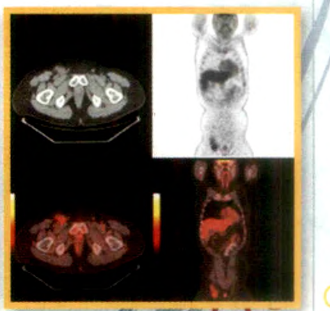
مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة



TOPICS:

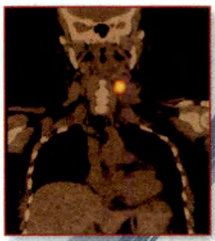
- Thyroid cancer
- Lymphoma
- Neuroendocrine Tumors
- Hepatic Tumors
- Others

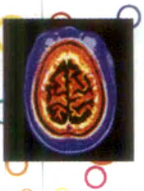


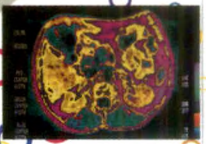


WHO SHOULD ATTEND:

Oncologists
Nuclear Medicine Physicians
Radiotherapists
Radiologists
Radiological Technologists and Nurses







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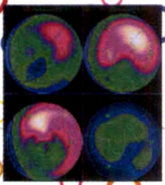
E-mail: eatizado@kfhsrc.edu.sa
Website : www.kfshrc.edu.sa/symposia



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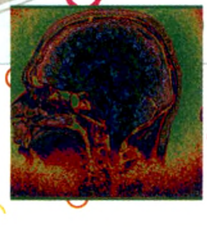

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الجرعات المُثلى من مثبط الأنزيم المحول للأنجيوتنسين لمرضى الفشل القلبي المزمن: دراسة مقطعية في فلسطين

مقدمة: لأن المعالجة باستخدام جرعات عالية من مثبط الأنزيم المحول للأنجيوتنسين أمر مستحب لمرضى الفشل القلبي المزمن، فقد سعينا لتحديد أنماط استخدام وجرعات مثبط الأنزيم المحول للأنجيوتنسين لمرضى الفشل القلبي المزمن في مستشفى حكومي بفلسطين.

المرضى والطرق: هذه دراسة مقطعية أجريت في الفترة ما بين سبتمبر ٢٠٠٦م و أغسطس ٢٠٠٧م شملت جميع المرضى الذين جرى تنويمهم لإصابتهم بفشل قلبي مزمن ونسبة تفريغ أقل من ٤٠٪. وبعد أن استبعدنا المرضى ممن لديهم موانع لاستعمال مثبط الأنزيم المحول للأنجيوتنسين أو الذين لا يتلقونه، قمنا بإحصاء عدد المرضى الذين يتلقون جرعات مُثلى (كابتوبريل ١٥٠-٣٠٠ ملغم يومياً، إنالابريل ٢٠-٤٠ ملغم يومياً، راميبريل ٥-١٠ ملغم يومياً) والذين يتلقون جرعات دون المُثلى. وبعد ذلك أجرينا تحليلاً إحصائياً لتقييم الترابط بين استعمال مثبط الأنزيم المحول للأنجيوتنسين وتحديد الجرعات وبين العوامل السكانية والسريرية المختلفة.

النتائج: من بين ١٦٥ مريضاً تم تقييمهم مبدئياً، كان هناك ٦٩ مريضاً (٤١,٨٪) لديهم موانع لاستعمال مثبط الأنزيم المحول للأنجيوتنسين (n=٢٨، ٤٠,٦٪) أو لم يكونوا يتلقونه (n=٤١، ٥٩,٤٪). ومن بين ٩٦ مريضاً المتبقين (٧٠,١٪). كان ٤٩ من أصل ٩٦ (٥١٪) يتلقون جرعة مُثلى، بينما ٤٧ من أصل ٩٦ (٤٩٪) يتلقون جرعة دون المُثلى. ومن بين جميع مرضى الفشل القلبي المزمن الذين ليست لديهم موانع لاستعمال مثبط الأنزيم المحول للأنجيوتنسين، كان ٨٨ (٦٤,٢٪) إما لا يتلقون مثبط الأنزيم المحول للأنجيوتنسين أو يتلقون جرعة دون المُثلى. كان العامل الوحيد الذي ترابط بشكل هام مع استعمال مثبط الأنزيم المحول للأنجيوتنسين هو الإصابة بارتفاع ضغط الدم (P=٠,٠٠٩، نسبة الأرجحية= ٢,٧). أما استعمال جرعة مُثلى فلم يكن مرتبطاً بشكل هام مع أي من العوامل التي تم اختبارها (العمر، الجنس، الإصابة بارتفاع ضغط الدم أو السكري أو خلل الكلى أو مرض قلبي إقفاري أو عدد من الأمراض الأخرى).

الاستنتاج: وجدنا أن الاستعمال الناقص لمثبط الأنزيم المحول للأنجيوتنسين وتلقي جرعات دون المُثلى كان أمراً شائعاً. وبما أن هناك الكثير من الأدلة المشجعة على المعالجة بمثبط الأنزيم المحول للأنجيوتنسين لمرضى الفشل القلبي المزمن، فإنه لابد من تثقيف الأطباء بشأن إعطاء الجرعات الصحيحة من هذه الأدوية.

تصليح الفتق المجاور للسرة أثناء الولادة القيصرية

مقدمة: عادة ما تقوم السيدات الحوامل بتأجيل عملية تصليح الفتق المجاور للسرة إلى ما بعد الولادة، إلا أن بعض السيدات يطلبن إجرائها أثناء الولادة القيصرية. لذا، فقد قمنا بتقييم نتائج الولادة القيصرية المشتركة مع عملية تصليح للفتق المجاور للسرة من خلال دراسة استطلاعية لدى مستشفى إحالة جامعي متخصص.

المرضى والطرق: من خلال دراسة استطلاعية، قمنا بمقارنة نتائج ٤٨ سيدة أجريت لهن الولادة القيصرية المشتركة مع تصليح الفتق المجاور للسرة مقابل ١٠٠حالة منخفضة الخطورة ممن أجريت لهن الولادة القيصرية فقط. كانت مقاييس النتائج هي الوقت المستغرق في إجراء الجراحة، مستوى فقدان الدم، حدة الألم، الفترة المحيطة بالولادة، فترة الإقامة بالمستشفى ومستوى رضا المريضات.

النتائج: استغرقت الجراحة المشتركة وقتا أطول بشكل ملحوظ عن الولادة القيصرية فقط (٧٥,٢ دقيقة مقابل ٦٠,٥دقيقة). لم تكن هناك أي مضاعفات خطيرة. فقد أصيبت ٦ سيدات بالتهابات في منطقة الجراحة (٤,١٪) . لم تختلف فترة التنويم في المستشفى بشكل كبير. وقد ظهر الألم في موقع جراحة تصليح الفتق لدى مريضتين، وتكرر ظهور الفتق لدى مريضة واحدة من المجموعة التي أجريت لها جراحة تصليح الفتق خلال فترة المتابعة الرئيسية والتي تبلغ ٢٢ شهرا (تتراوح بين ٦-٣٦شهرا). وقد ذكرت جميع السيدات بأنهن فضلن العملية المشتركة.

الاستنتاج: تتميز الولادة القيصرية المشتركة مع عملية تصليح الفتق المجاور للسرة بميزة الشق الواحد، والتخدير لمرة واحدة، والإقامة لفترة واحدة في المستشفى مع تجنب إعادة التنويم لإجراء عملية تصليح منفصلة للفتق. تشير نتائجنا إلى أمان هذه الوسيلة المشتركة، وفعاليتها وقبولها بشكل جيد.

أنظمة الدوران خارج الجسم أثناء نقل الحالات الحرجة بين المستشفيات: خبرة مستشفى واحد

المقدمة والأهداف: لا يمكن نقل المرضى الذين هم في حالة حرجة ومصابين بقصور دوراني حاد إلى مستشفيات أخرى ما لم تستقر حالاتهم باستعمال أنظمة مساعدة ميكانيكية. وتستخدم الأنظمة المساعدة للقلب والرئة خارج الجسم بصورة متزايدة كجسر ريثما يتحقق شفاء العضو أو تجرى عملية زراعة وكوسيلة إنقاذية أخيرة في الإنعاش القلبي الرئوي.

المرضى والطرق: خلال الفترة من يوليو ٢٠٠١م إلى إبريل ٢٠٠٨م تسلمنا ٣٨ طلبا لمساندة خارج الجسم من أجل نقل مرضى بين المستشفيات بواسطة الخدمات الطبية الجوية. كان هناك قصور تنفسي لدى ٢٩ مريضا تم تزويدهم بأنظمة مساعدة عديمة المضخة للرئة خارج الجسم PELCA أو أكسجة غشائية وريدية - وريدية خارج الجسم ECMO. سيطر القصور القلبي لدى ٩ مرضى تلقوا مساندة حياتية خارج الجسم ECLS. كانت الأمراض الأساسية هي متلازمة الضائقة التنفسية الحادة لدى ١٥ مريضا، وذات الرئة لدى ٧، ورئة مزروعة سابقا لدى ٤، وصدمة قلبية المنشأ لدى ٧، وصدمة إنتانية لدى ٤.

النتائج: تم توصيل جميع الأنظمة المساعدة من خلال أوعية محيطية بطريقة سيلدينجر. تم النقل بدون متاعب في جميع الحالات وبدون فشل فني. أصيب مريضان بنقص تروية الساق لدى وصولهما إلى مستشفى العناية المتخصصة، وتم تغيير موضع الأنبوب الشرياني. وبعد فترة مساندة متوسطها (الانحراف المعياري) ٥,١ (٣,٠) يوما للأنظمة المساعدة PELCA و٣,٥ (٢,٩) يوم للمساندة الحياتية ECLS، و٧,٣ (٥,٨) أيام للأكسجة الغشائية ECMO أمكن بنجاح فصل ما نسبته ٦٠٪ و٦٦٪ و٦٦٪ من المرضى عن الأجهزة على التوالي. كانت معدلات الخروج من المستشفى ٤٥٪ للأنظمة المساعدة PELCA و٤٤٪ للمساندة الحياتية ECLS و٥٦٪ للأكسجة الغشائية ECMO.

الاستنتاج: تثبت خبرتنا أن الأجهزة المساعدة المصغرة الموجودة خارج الجسم توفر مساعدة مأمونة للمرضى الذين يعانون من قصور رئوي وقلبي معزول أو مختلط والذين يحتاجون إلى نقل بين المستشفيات. وبالتالي توفر للحالات الحرجة فرصة الوصول إلى مركز عناية طبية قصوى.

علاج الإصابات الرضيّة في الشريان العضدي: تقرير شمل ٤٩ مريضاً

مقدمة: الشريان العضدي هو أكثر الشرايين تعرضاً للإصابة في الطرف العلوي بسبب سرعة تأثره. الهدف من هذه الدراسة هو عرض تجربتنا عن إصابات الشريان العضدي خلال تسع سنوات، وذلك بوصف نوع الإصابة، العمليات الجراحية، المضاعفات، والإصابات المصاحبة له.

المرضى والطرق: خضع تسع وأربعون من المرضى الذين يعانون من إصابة في الشريان العضدي لعمليات إصلاح جراحية بمستشفانا، وذلك من فترة مايو ١٩٩٩م إلى يونيو ٢٠٠٨م. وتم تشخيص إصابات الشريان العضدي بواسطة الفحص الجسدي وفحص دوبلر. بناء على نوع الحالة، تم إما نقل المرضى فوراً إلى غرفة العمليات للتحكم بالنزف وإجراء عملية إصلاح للأوعية، أو تقييمهم بواسطة إجراء تخطيط الجريان بدوبلر الموجات فوق الصوتية قبل العملية.

النتائج: شملت هذه الدراسة ٤٣ من الذكور و ٦ من الإناث، تتراوح أعمارهم من ٦ إلى ٦٥ سنة، والمتوسط المعياري للفئة العمرية ٢٧,٩ (٦,٧) عاماً. كانت الآلية المتسببة بالرض حادة في ٤٥ حالة من المرضى وغير حادة في الحالات الأربعة المتبقية من المرضى. الإصابة بالطعن كانت أكثر أشكال الإصابة الحادة حدوثاً (٢٤ من ٤٥). شمل العلاج إصلاح الشرايين الرئيسية في ٥ حالات، مفاغرة النهايات في ٢٨ حالة، توضيع بيني لطعم وريدي في ١٥ حالة، توضيع بيني لطعم "بولي تترافلوروإيثيلين" حلقي في حالة واحدة.

الاستنتاج: إن العلاج الفوري والملائم لإصابات الشريان العضدي، والاهتمام بالإصابات المصاحبة له، والاستعداد لمراجعة عملية إصلاح الأوعية باكراً لدى حدوث قصور، سيزيد من نسبة بقيا المريض وإنقاذ الطرف العلوي.

موثوقية ومصداقية النسخة القصيرة من استبيان نوعية الحياة لمنظمة الصحة العالمية لدى عينة من السكان العرب

المقدمة والأهداف: ثمة اهتمام متزايد في أبحاث نوعية الحياة في البلاد العربية. الهدف من هذه الدراسة هو تقييم موثوقية ومصداقية النسخة القصيرة من استبيان نوعية الحياة لمنظمة الصحة العالمية لدى عينة من المواطنين على مستوى دولة الكويت، وهو استبيان يستخدم على نطاق واسع، ويتكون من ٢٦ بندا تغطي مجالات الصحة البدنية والصحة النفسية والعلاقات الاجتماعية والبيئة.

الطرق: أجابت عن النسخة العربية للاستبيان عينة اختيرت بشكل عشوائي منهجي متناسب (واحد من ثلاثة) من المواطنين الكويتيين الموافقين الذين يعملون في المخازن التعاونية الكبيرة والمكاتب الحكومية البلدية في ست محافظات. شملت المناسب التي تم تقييمها موثوقية الفحص - إعادة الفحص، التوافق الداخلي، التوافق الداخلي للبند، مصداقية التمييز للبند، مصداقية المجموعات • المعروفة، مصداقية البناء.

النتائج: ضمت الدراسة ٣٣٠٣ مشاركا (٤٤٫٨٪ ذكور، ٥٥٫٢٪ إناث، العمر المتوسط ٣٥٫٤ سنة، المدى ١٦ إلى ٨٧ سنة). كان معامل كرونباتش ألفا › ٠٫٧ للترابط داخل الفئة لمفردة الفحص • إعادة الفحص ولقيم التوافق الداخلي للاستبيان كله والمجالات. ومن بين ٢٤ بندا تؤلف المجالات استوفى ٢١ بندا شرط التوافق الداخلي للبند بأن يكون الترابط › ٠٫٤ مع المجال المطابق في حين أن ١٦ بندا استوفت معيار مصداقية التمييز للبند بأن يكون ترابطها أعلى مع المجال المطابق من المجالات الأخرى. علامات المجال ميزت بدرجة مهمة بين مجموعتي الأصحاء والمرضى. أما في تحليل العوامل فقد برزت أربعة عوامل قوية بنفس البناء كما هو في تقرير منظمة الصحة العالمية.

الاستنتاج: تمتاز الترجمة العربية للنسخة القصيرة من استبيان نوعية الحياة لمنظمة الصحة العالمية بمناسب مصداقية وموثوقية تبعث على الإعجاب. أما انخفاض مصداقية التمييز للبند فهي ناجمة عن الطبيعة متعددة الأبعاد للاستبيان. ومن المفترض أن تطمئن مناسب المصداقية المرتفعة الباحثين إلى أن الاستبيان يمثل نفس البناءات عبر الثقافات. قد تكون هناك حاجة إلى تحسين البنود المصاغة بطريقة سلبية.

معاودة فيروس التهاب الكبد ج النمط الجيني-٤ الذي يلي عملية زراعة الكبد سوية الموضع: تاريخ طبيعي ومؤشرات للنتائج

مقدمة: لم نجد إلا بضعة تقارير قليلة عن معاودة التهاب الكبد ج النمط الجيني -٤(HCV-٤) بعد زراعة الكبد سوية الموضع (OTL). لذا، فقد أجرينا الدراسة لتحديد السمات الوبائية، السريرية والفيروسية لدى المرضى الذين ثبتت معاودة فيروس التهاب الكبد ج لديهم بالخزعة وتحليل العوامل التي تؤثر على شدة معاودة المرض. كما قمنا بمقارنة معاودة المرض مع مقارنة نتائج فيروس HCV-٤ والأنماط الجينية الأخرى.

المرضى والطرق: تم التعرف على جميع المرضى ممن أجريت لهم زراعة كبد سوية الموضع (في المملكة أو في الخارج) لمعاناتهم من فيروس التهاب الكبد ج ابتداء من ١٩٩١م وحتى ٢٠٠٦م والذين عانوا من معاودة فيروس التهاب الكبد ج. وتم جمع البيانات السريرية والخبرية والباثولوجية وتحليلها قبل خضوعهم لعملية الزراعة وبعدها.

النتائج: كان من ضمن ١١٦مريضا أجريت لهم عملية زراعة كبد سوية الموضع لإصابتهم بفيروس التهاب الكبد ج.٤٦(٣٩,٧٪) الذين تطابقت حالاتهم مع معايير معاودة فيروس التهاب الكبد ج. تسعة وعشرون (٦٣٪)كانوا مصابين بفيروس التهاب الكبد ج من النمط الجيني ٤. كان متوسط العمر (الانحراف المعياري) ٥٤,٩ (١٠,٩)سنه. ١٩ منهم كانوا ذكورا (٦٥,٥). ٢١(٧٢,٤) أجريت لهم زراعة كبد من متوفى دماغيا، و٧ (٢٤,١٪) أصيبوا بنوبة رفض حادة أو أكثر. من الناحية الباثولوجية، ٧ (٢٤,١٪) و٤ (١٣,٨٪) عانوا من الالتهاب من الدرجة ٣-٤، على التوالي. وأظهرت نتائج الخزعة لدى ٩(٣١٪) من المرضى استقرارا، أو تليفاً أسوأ مع تحسناً في المرحلة لدى مريضين وخمسة ومريضين على التوالي. ومن بين ٧مرضى من المجموعة التي عانت من معاودة فيروس التهاب الكبد ج ممن توفوا، كان ستة منهم مصابين بالنمط الجيني ٤ وأربعة منهم توفوا نتيجة لأسباب متعلقة بفيروس التهاب الكبد ج.

الاستنتاج: يشير هذا التحليل إلى أن معاودة فيروس التهاب الكبد ج بعد عملية زراعة الكبد سوية الموضع لدى المرضى المصابين HCV-٤ لا يختلف كثيرا عن معاودة الأنماط الجينية الأخرى.

الخلاصات العربية

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تصدر المدونات الطبية السعودية مرة كل شهرين عن مستشفى الملك فيصل التخصصي ومركز الأبحاث ، ص.ب ٣٣٥٤ ، الرياض ١١٢١١، المملكة العربية السعودية. يتم توزيع المدونات وإعداد الملخصات العربية بالتعاون مع د. زهير القاوي بواسطة موظفي إدارة الخدمات الإدارية بمستشفى الملك فيصل التخصّصي ومركز الأبحاث. جميع المراسلات والاستفسارات وطلبات الاشتراك ترسل إلى المحرر الأول مكتب المطبوعات (ر.إ ٣٦). سعر الاشتراك ١٠٠ ريال في السنة للأفراد داخل المملكة و٢٠٠ ريال في السنة للأفراد خارج المملكة و٥٠٠ ريال في السنة للمؤسسات. يمكن فتح اشتراك مجاني للأفراد و المؤسسات في الدول النامية. ترسل طلبات الاشتراك أو إلغاء الاشتراك الى البريد الإلكتروني: admin@saudiannals.com

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المدونات الطبية السعودية ر.إ (٣٦)
مستشفى الملك فيصل التخصّصي ومركز الأبحاث .
ص.ب ٣٣٥٤
الرياض ١١٢١١
المملكة العربية السعودية
هاتف: ٤٦٤٧٢٧٢-١-٩٦٦ تحويلة ٣١٨١٩/٣١٨١٥
فاكس: ٤٦٤٧٢٧٢-١-٩٦٦ تحويلة ٣١٨٧٥
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الرقم التسلسلي القياسي الدولي: ٠٢٥٦ - ٤٩٤٧
١٤٢٧-٠٤

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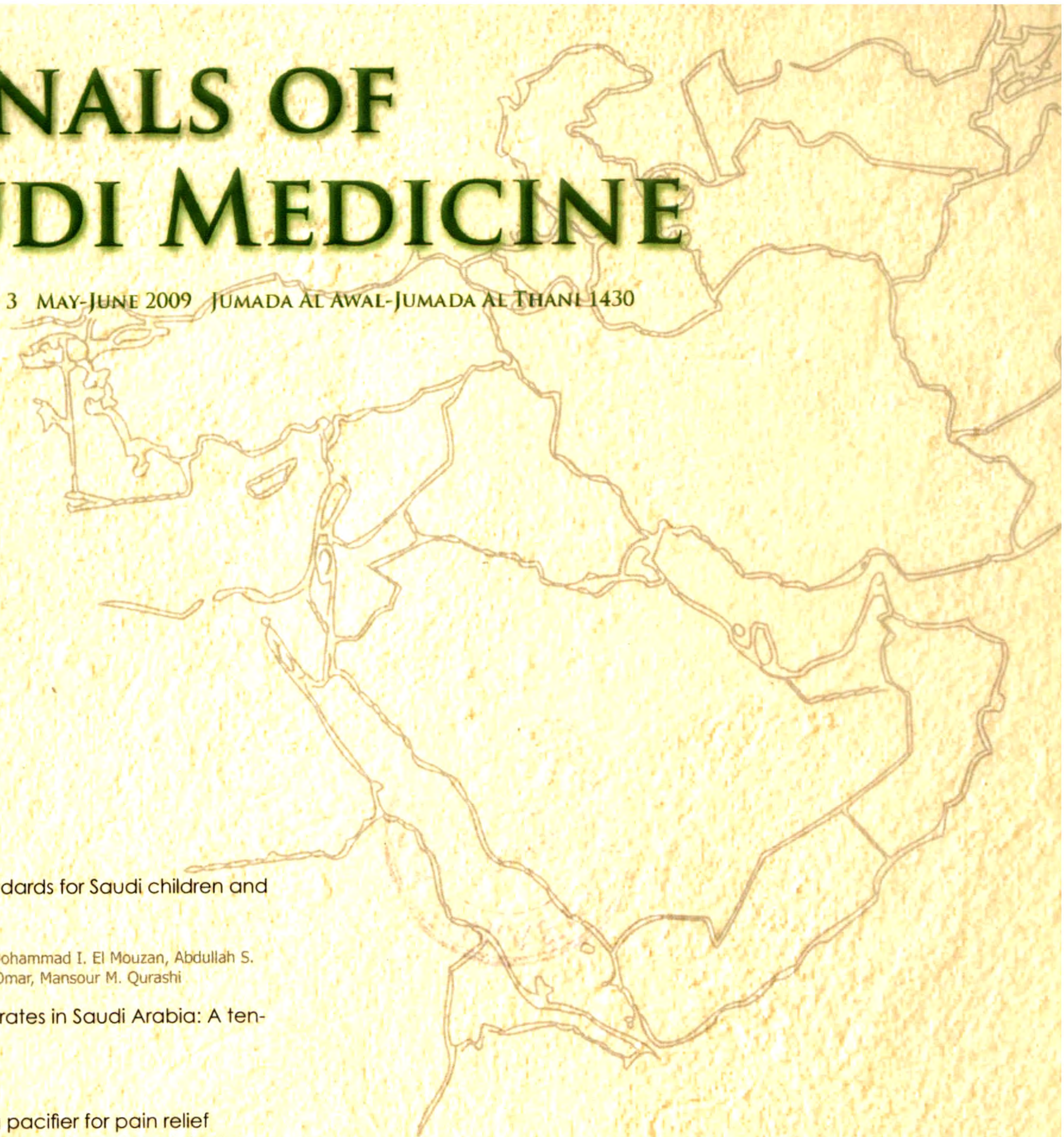
VOLUME 29 ISSUE 3 MAY-JUNE 2009 JUMADA AL AWAL-JUMADA AL THANI 1430



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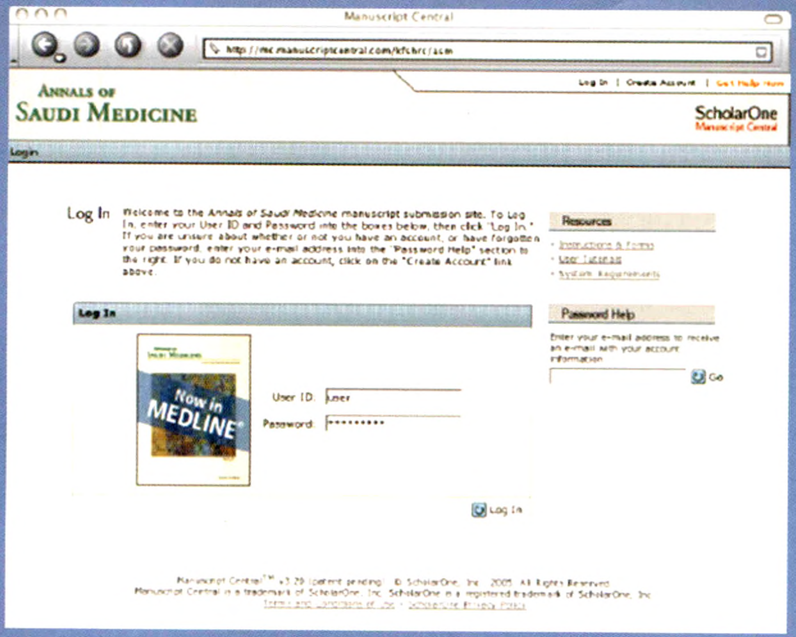

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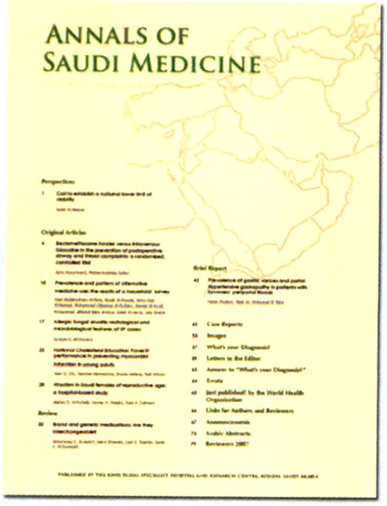

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P.O. Box 995
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The *Annals of Saudi Medicine* is published bimonthly by King Faisal Specialist Hospital & Research Centre. Arabic abstracts are prepared, in association with Dr. M. Zuheir Al-Kawi, by the staff of the Office Services Department of King Faisal Specialist Hospital & Research Centre.

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OBITUARY

Dr. Kamal A. Hanash
1940-2009

Kamal A. Hanash, MD, completed medical school at the American University Beirut in 1966. He then graduated in urology from the Mayo Clinic in 1970. His MS in Urology was obtained at the University of Minnesota in 1974. As a board certified urologist, Dr. Hanash was also a member of the International Advisory Board of the Glickman Urological Institute at the Cleveland Clinic, and Clinical Professor of Urology at Georgetown University Medical Center in Washington, DC. Dr. Hanash was the author of 4 books, 13 chapters in medical books and had published more than 80 papers in peer-reviewed medical journals. He also participated in public education over the past 7 years in the form of a weekly medical page in a Riyadh newspaper. Dr. Hanash was the Editor-in-Chief of the *Annals of Saudi Medicine* from 1980 to 1984. Half of his 39 years of work experience was spent in the United States and Lebanon, and the other half as Chairman of the Department of Urology at King Faisal Specialist Hospital & Research Centre in Riyadh.

I have known Dr. Hanash as a dedicated, high-profile urologist for the past 30 years. The first time I met him was in late 1979 when we were initiating the Riyadh Urology Club meeting, which is still held every month. Dr. Hanash was one of the 17 urologists in Saudi Arabia who were the founding members of the annually organized Saudi Urological Conference (SUC) in 1982. Dr. Hanash organized and chaired the 16th SUC in 2004 and was going to chair the 22nd SUC in March 2010. Dr. Hanash's contribution to Saudi urology was magnificent. During his 20 years of service (1979-1985, 1995-2009) as an active and very energetic senior urologist, he was an icon for many urologists who worked with him. In addition to his excellent urological performance, Dr. Hanash made major contributions to postgraduate education, training and research. With the demise of Dr. Hanash, the Saudi urological community and patients have lost an outstanding urologist, educator and teacher.

Dr. Mohammed S. Abomelha
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SUMMARIES

PEDIATRICS

Blood pressure standards for Saudi children and adolescents

Using data from a house-to-house survey of 16 226 subjects in all 13 regions of Saudi Arabia, Al Salloum and colleagues developed reference values for systolic and diastolic blood pressure for Saudi children and adolescents. Blood pressure rose steadily with age in both boys and girls. Values for the 90th percentile differed from those in American and Turkish children, indicating that comparisons across studies are difficult and that every population should use their own normal standards to define blood pressure levels in children.

OBSTETRICS/GYNECOLOGY

Cesarean delivery rates in Saudi Arabia: A ten-year review

Ba'aqeel found that cesarean delivery rates rose 80.2% in Saudi Arabia from 1997 to 2006, using maternity data from Ministry of Health hospitals but not private hospitals. The greatest increase of 265% was in the Northern region and the least of 32.8% was in the Royal Commission Hospitals. A strategy to reduce the cesarean delivery rate is needed. The author recommends that the vital registration system be upgraded and that national data capturing mechanisms be expanded to include private sector data and to record indications for cesarean delivery.

PEDIATRICS

Oral sucrose and a pacifier for pain relief during simple procedures in preterm infants: a randomized controlled trial

Elserafy and colleagues randomly allocated 36 preterm infants (gestational age, 27 to 36 weeks) to six different regimens of sucrose solution (24%) or sterile water with or without pacifier, or pacifier alone or a control group during a stay in intensive care up to 15 days. The lowest pain scores occurred with the use of the sucrose solution combined with the pacifier. The synergistic effect of the sucrose solution and pacifier was clinically effective and safe in relieving the pain of simple procedures such as venipuncture or heel stick, but further research is needed on these interventions alone and in combination with other behavioral interventions in neonates.

RHEUMATOLOGY

Extra-articular manifestations of rheumatoid arthritis: a hospital-based study

Al-Ghamdi and Attar found that 98 of 140 patients (70%) with rheumatoid arthritis developed extra-articular manifestations in a retrospective study of patients diagnosed over a 4-year period at a university hospital. Anemia occurred in 61%, pulmonary involvement in 10%, renal amyloidosis in 6%, vasculitis in 2% and Felty syndrome in 1%. The mortality rate was high (16%) in patients with extra-articular manifestations. Predictors of mortality were lung involvement, age over 50 years and kidney amyloidosis. Early recognition and treatment are important to decrease the mortality rate.

DIABETES

Anthropometric predictors of incident type 2 diabetes mellitus in Iranian women

In 2801 females aged ≥21 years who were non-diabetic or had abnormal glucose tolerance at baseline, Hadaegh and colleagues examined predictors for the development of diabetes using a multivariate model that adjusted for age, hypertension, triglyceride levels, HDL-cholesterol, family history of diabetes, and abnormal glucose tolerance. Over a median follow-up of 3.5 years, 114 women (4.1%) developed diabetes. They found that weight-to-height ratio was a better predictor for the development of diabetes than body mass index.

original article

Blood pressure standards for Saudi children and adolescents

Abdullah A. Al Salloum,[a] Mohammad I. El Mouzan,[a] Abdullah S. Al Herbish,[a] Ahmad A. Al Omar,[b] Mansour M. Qurashi[c]

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Ann Saudi Med 2009; 29(3): 173-178

BACKGROUND AND OBJECTIVES: Blood pressure levels may vary in children because of genetic, ethnic and socioeconomic factors. To date, there have been no large national studies in Saudi Arabia on blood pressure in children.Therefore, we sought to establish representative blood pressure reference centiles for Saudi Arabian children and adolescents.

SUBJECTS AND METHODS: We selected a sample of children and adolescents aged from birth to 18 years by multi-stage probability sampling of the Saudi population. The selected sample represented Saudi children from the whole country. Data were collected through a house-to-house survey of all selected households in all 13 regions in the country. Data were analyzed to study the distribution pattern of systolic (SBP) and diastolic blood pressure (DBP) and to develop reference values. The 90th percentile of SBP and DBP values for each age were compared with values from a Turkish and an American study.

RESULTS: A total of 16 226 Saudi children and adolescents from birth to 18 years were studied. Blood pressure rose steadily with age in both boys and girls. The average annual increase in SBP was 1.66 mm Hg for boys and 1.44 mm Hg for girls. The average annual increase in DBP was 0.83 mm Hg for boys and 0.77 mm Hg for girls. DBP rose sharply in boys at the age of 18 years. Values for the 90th percentile of both SBP and DBP varied in Saudi children from their Turkish and American counterparts for all age groups.

CONCLUSION: Blood pressure values in this study differed from those from other studies in developing countries and in the United States, indicating that comparison across studies is difficult and from that every population should use their own normal standards to define measured blood pressure levels in children.

The assessment of blood pressure (BP) and prevention of hypertension in children and adolescents has become a worldwide priority.[1] Childhood blood pressure is predictive of adult blood pressure.[2] Therefore, measurement of blood pressure is considered to be an integral part of the clinical examination.[3] To define a standard for blood pressure in children, the Task Force on Blood Pressure Control in Children in the United States published a series of reports on blood pressure levels related to age, height and weight from birth to 18 years.[4-6] The distribution of blood pressure levels and the prevalence of hypertension vary in different racial and ethnic groups.[7-11] The variation is dependent upon a multitude of factors, both genetic and environmental.[4] Based on these variations, reference norms developed for one particular population may not be applicable to others.[7-10] Local reference data are essential to evaluate observed blood pressure values.

A number of epidemiological studies have established normal blood pressure values in different populations,[12] but few are from developing countries.[7,8,13] To our knowledge, there are no blood pressure reference data on Arab children based on a nationwide survey. This study was designed to provide age-related blood pressure reference standards for Saudi Arab children.

METHODS

Our study was part of the Health Profile of the Saudi Arabian Children and Adolescents project, which was a house-to-house survey of 14 000 randomly selected households from all provinces in Saudi Arabia, including urban and rural areas. Households were randomly selected by a multi-stage probability sampling pro-

Table 1. Smoothed percentiles of systolic blood pressure for boys (1-18 years).

Age (years)	Number	50th	75th	90th	95th
1	598	93	99	106	109
2	403	95	101	108	112
3	453	97	104	110	114
4	502	99	105	112	116
5	545	101	107	114	117
6	497	103	109	115	119
7	555	104	110	117	121
8	508	105	112	118	122
9	501	107	113	120	123
10	557	108	114	121	125
11	536	110	116	122	126
12	472	111	117	124	127
13	458	113	119	125	129
14	439	114	120	127	131
15	389	116	122	129	132
16	374	118	124	130	134
17	293	120	126	133	137
18	218	123	129	135	139

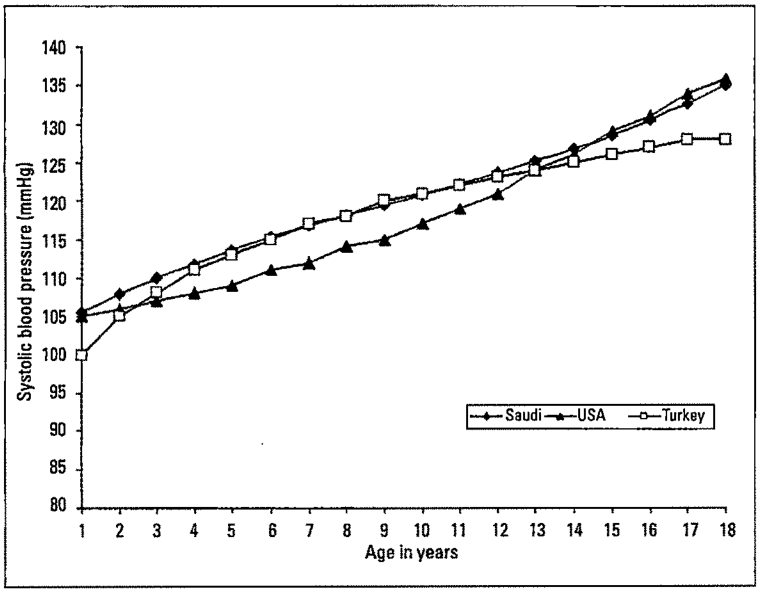

Figure 1. Comparison of the 90th percentile of systolic blood pressure levels of Saudi Arab boys with the values of American[4] and Turkish[7] boys.

cedure from a stratified listing based on the updated 2000-2001 census. This computerized process was performed with the assistance of the General Directorate of Statistics, Ministry of Planning, who provided details of the selected households in cities and villages, including road and street maps. A sub-sample was selected randomly from the original main sample to measure blood pressure. Workshop training of field teams was conducted in each of the 13 regions of the country. The workshops included oral presentations and small group training on procedures for locating selected households, explanations of the questionnaire, family interviews, clinical examinations of the children and the taking of measurements and recording of data. The training included practical demonstrations to members of the field teams on how to use and maintain the blood pressure measurement devices.

Specific guidelines in Arabic and English were provided to the members of the teams. Each team consisted of one physician and one to two female nurses. The clinical examination of the children and adolescents was performed by the physicians to determine eligibility for measurements. Only healthy children and adolescents as determined by interview, clinical examinations and anthropometric measurements were eligible for measurement of BP. The survey questionnaire was designed to provide basic information about the subject, including birth date, perinatal history, nutrition, childhood illnesses, socioeconomic status of the family and body measurements. The exact birth date was considered to be particularly important and acceptable only when it was completely recorded from an official document. The exact date of measurement was also noted, both dates essential for the determination of the exact age at the time of measurements.

Electronic devices using oscillometric techniques were used in the study. The devices fulfilled the American Association for the Advancement of Medical Instrumentation (AAMI), and were graded A for both systolic and diastolic pressure under the British Hypertension Society (BHS) protocol, as recommended by the European Society of Hypertension.[14] All the devices were new and purchased especially for the study (Accutorr Plus, Datascope Corp, NJ, USA). The cuff was appropriate to the size of the upper arm according to the standard technique recommended by the working group report from the National High Blood Pressure Education Program.[4,5] The right arm was used for consistency in comparison with other studies. Two readings, one at the end of the interview and the other at the end of the physical examination, were performed for each subject with an interval of 5 minutes and in the presence of both parents. For children younger than 2 years, the readings were taken in the supine position and for children older than 2 years, the readings were taken in the sitting position. The lowest of the two readings was recorded for the final analysis. A pilot study was performed to test all the components of the project before the actual start of the main study.

Data collection was performed over a period of 2 years (2004-2005) by house-to-house visits. Precautions were taken to ensure reliability and accuracy of measurements. In addition to the use of equipment known for high accuracy, intra- and inter-observer reliability were tested by selection of 1% of the children to be re-measured by the same or another observer. Multiple frequency analysis was used to detect any missing data, inconsistencies and other types of errors. All questionable data were double-checked.

The SAS system software was used. Descriptive statistics (mean, standard deviation and percentiles) were used to explore the data. Correlation and simple regression analysis were used to assess the linear relationship between two continuous variables. All values were related to the age and sex of the children. The criteria used to establish normal and abnormal were similar to those of the Second Task Force report on blood pressure control in children (normal 50th-90th percentile), (high normal 90th-95th percentile), (high >95th percentile).[4,5]

RESULTS

A total of 16 226 Saudi Arabian children (7928 girls and 8298 boys) from birth to 18 years of age were examined in this study. Smooth percentile values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) for these children according to age and sex are shown in Tables 1-4. SBP and DBP rose steadily with age in both boys and girls. The average annual increase in SBP for boys was 1.66 mm Hg and 1.44 mm Hg in girls (Table 1, 2). There was no significant differences in the increment in pre-pubertal and pubertal age group in boys, while in girls the SBP increment was 1.77 mm Hg up to the age of 9 years and it then decreased to 1 mm Hg/year from 10 to 18 years (Table 2). The corresponding increments were higher for girls than boys in the first 9 years of life. The average annual increases in DBP throughout childhood and adolescence for boys and girls were 0.83 mm Hg and 0.77 mm Hg, respectively (Tables 3, 4). Of note, the DBP in boys rose sharply at the age of 18 years (Table 3), which is probably related to the stress associated with this age group. The 90th percentile of SBP and DBP values in this study were compared for each age with the 90th percentile of SBP

Table 2. Smoothed percentiles of systolic blood pressure for girls (1-18 years).

Age (years)	Number	50th	75th	90th	95th
1	573	93	100	106	110
2	393	95	102	109	113
3	468	98	105	111	115
4	476	100	107	114	117
5	495	102	109	116	119
6	469	104	111	117	121
7	540	105	113	119	123
8	474	107	114	121	125
9	498	109	116	122	126
10	524	110	117	124	128
11	451	111	118	125	129
12	437	112	120	126	130
13	422	113	121	127	131
14	439	114	122	128	132
15	364	115	123	129	133
16	352	116	124	130	134
17	309	117	124	131	135
18	244	118	125	132	136

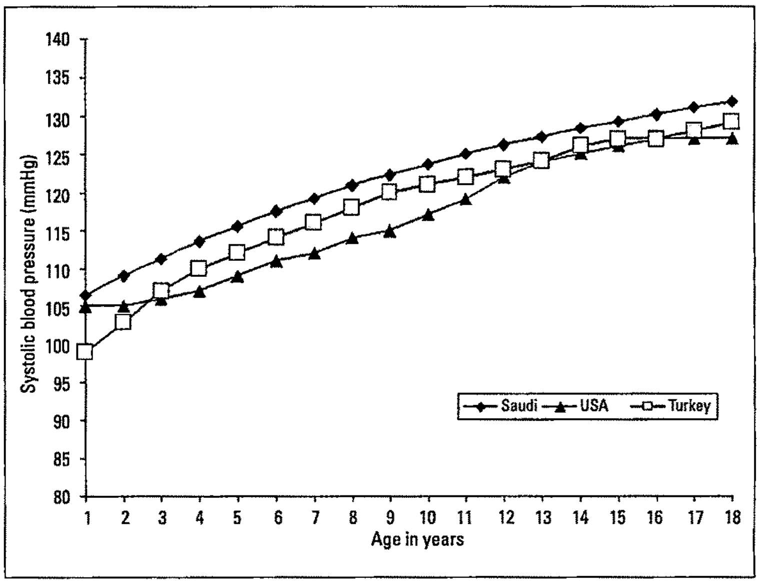

Figure 2. Comparison of the 90th percentile of systolic blood pressure levels of Saudi Arab girls with the values of American[4] and Turkish[7] girls.

Table 3. Smoothed percentiles of diastolic blood pressure for boys (1-18 years).

Age (years)	Number	50th	75th	90th	95th
1	598	57	63	68	72
2	403	59	65	70	74
3	453	60	66	72	75
4	502	62	68	73	77
5	545	63	69	74	78
6	497	64	70	76	79
7	555	65	71	76	80
8	508	66	72	77	80
9	501	66	72	78	81
10	557	67	73	78	82
11	536	67	73	79	82
12	472	68	74	79	83
13	458	68	74	80	83
14	439	69	75	80	84
15	389	70	76	81	84
16	374	70	76	82	85
17	293	71	77	82	86
18	218	72	78	83	89

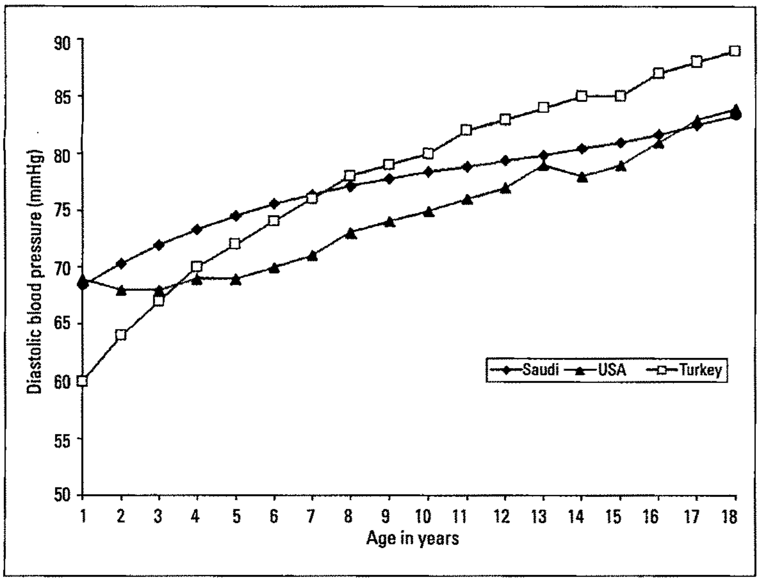

Figure 3. Comparison of the 90th percentile of diastolic blood pressure levels of Saudi Arab boys with the values of American[4] and Turkish[7] boys.

and DBP reported by one international study[4] and one regional study[7] (Figures 1-4). The 90th percentile of SBP in boys was closer to the Turkish levels for the age group of 5-11 years, and both are higher than the levels in the American study (Figure 1). For the ages of 14 to 18 years Saudi and American levels were significantly higher than those of the Turkish children. The 90th percentiles for SBP measurement for Saudi girls were higher than for their American and Turkish counterparts in all age groups (Figure 2). The 90th percentiles for DBP in Saudi boys were higher than both American and Turkish children in the first 6 years of life, and then became lower than in Turkish children. By the age of 16 years the level of DBP in American and Saudi children were closer to each other, but significantly lower than the Turkish levels (Figure 3). A similar pattern was noted for DBP in girls (Figure 4).

DISCUSSION

The incorporation of blood pressure measurement into the routine pediatric examination as well as the publication of national norms for blood pressure in children not only enables detection of significant asymptomatic hypertension secondary to a previously undetected disorder, but also confirms that mild elevation in blood pressure during childhood is more common than previously recognized, particularly in adolescents.[2,6] It is now understood that hypertension detected in some children may be a sign of an underlying disease, such as renal parenchymal disease, whereas in other cases elevated blood pressure may represent the early onset of essential hypertension.[5]

The standard blood pressure percentile tables for children and adolescents provide arterial pressure values frequently seen in a large numbers of subjects presumed to be normal. Reference norms developed for one particular population may not be applicable to another because of racial, ethnical and cultural differences across the world.[15] The local reference data is essential to evaluate any observed blood pressure values. A number of epidemiological studies have established normal blood pressure values in different populations.[12] Combined data from several studies on references for blood pressure have been published from studies performed in the United States[4-6] and Europe.[16] The blood pressure percentiles presented here are based on data collected using a consistent and rigorous method in a representative sample of 16226 children and young people living in Saudi Arabia.

The definition of normal blood pressure values in children is based on mercury sphygmomanometry.[4-6] Accurate blood pressure measurement by mercury sphygmomanometry is particularly difficult in children because of widespread misinterpretations of the Korotkov sounds.[4,6,15,17-19] To overcome this problem and to eliminate human error, we used automated oscillometric devices, which represent a relatively new technology for blood pressure measurement.[20] The device is easy to use with small children because there is no need for auscultations.[20,21] Oscillometry is widely accepted in hospitals. Both systolic and diastolic pressures are calculated from measured mean artrial pressure in a sufficiently accurate manner.[20] These devices continue to gain wider use.[20] Earlier oscillometric devices often overestimated blood pressure compared with mercury sphygmomanometry, but newer models produce estimations of blood pressure that are very close to those of mercury sphygmomanometry,[15] particularly after the introduction of validation protocols by the American Association for the Advancement of Medical Instrumentation (AAMI) and the British Hypertension Society (BHS).[20] Some investigators have suggested that oscillometric devices might be superior to the auscultatory method, particularly in children, as a result of increased accuracy, reduced variability and ease of use.[12,15,20,22] Mercury sphygmomanometry, although conventionally regarded as the reference method, has inherent variability as a result of technique and human error, which has not been assessed comprehensively.[15] For optimal results, we used oscillometric devices that fulfill the AAMI criteria and are graded A for both SBP and DBP under the BHS protocol, and recommended by the European Society of Hypertension.[14]

Clinic blood pressure measurements tend to be higher than home measurements,[23] a phenomenon known as "white coat hypertension".[15] To record the real normal blood pressure for the subject by eliminating the effect of the "white coat", the measurement should be obtained in " normal circumstances" for the subject. We believe that the normal circumstances for the child is the home, which is certainly more comfortable to the child than the health hall at the school or the medical center. Most of the studies from which the working group Task Force derived their data are from a single measurement.[4] The first (or single) readings are usually higher than the average of multiple readings.[20] The average of multiple blood pressure readings is closer to basal blood pressure levels.[5] In our stud,y blood pressure measurements were based on the lowest of two measurements within five minute intervals. We believe that there is no need for additional effort to obtain more than two readings, once the child realizes, with the support of his family, the painless and benign nature of the procedure.

Table 4. Smoothed percentiles of diastolic blood pressure for girls (1-18 years).

Age (years)	Number	50th	75th	90th	95th
1	573	57	63	69	72
2	393	59	65	71	74
3	468	61	67	73	76
4	476	63	69	74	78
5	495	64	70	76	79
6	469	65	71	77	80
7	540	66	72	78	81
8	474	67	73	78	82
9	498	67	73	79	82
10	524	68	74	79	83
11	451	68	74	80	83
12	437	68	74	80	83
13	422	69	75	80	83
14	439	69	75	80	84
15	364	69	75	81	84
16	352	70	76	81	85
17	309	70	76	82	85
18	244	71	77	83	86

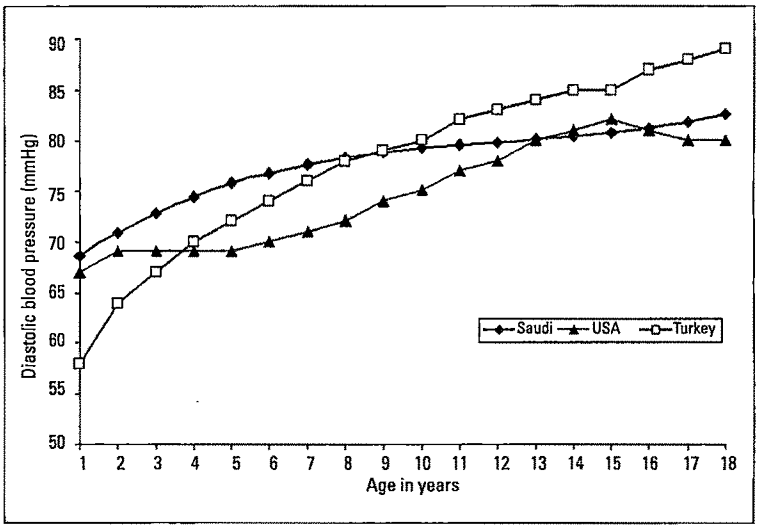

Figure 4. Comparison of the 90 percentile of diastolic blood pressure levels of Saudi Arab girls with the values of the American[4] and Turkish[7] girls.

It is of interest to compare our results statistically with those of other studies in other developing countries or in the United States, but it should be noted that the comparison of blood pressure values across these studies is difficult, since different criteria were employed.[4,7,8] In conclusion, these data on blood pressure measurements are the most recent, comprehensive and representative of the Saudi Arab population of children and adolescents. To our knowledge, this is the biggest prospective study of blood pressure in one of the developing countries. This reference data should help practicing clinicians in a better assessment of their patients blood pressure than the respective standards of other populations.

Acknowledgments

This study was approved and funded by King Abdulaziz City for Science and Technology (KACST). Grant number: AR-20-63. The authors thank KACST for the generous funding and support throughout the study. The authors express their thanks and appreciations to Dr. Kevin Sullivan, Atlanta, USA, for the data evaluation and analysis. Special thanks to all families, children and health teams who participated in this study.

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original article

Cesarean delivery rates in Saudi Arabia: A ten-year review

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Ann Saudi Med 2009; 29(3): 179-183

BACKGROUND AND OBJECTIVES: In view of the global increase in the rate of cesarean deliveries (CD), with the associated higher morbidity and mortality, this study was undertaken to review CD rates and some of their determinants over a ten-year period in Saudi Arabia.
METHODS: Maternity data for Ministry of Health (MOH) hospitals across 14 administrative regions and other governmental hospitals in nine clusters were collected and the corresponding rates calculated using MOH yearly statistical books from 1997 to 2006. No private hospital data are reported.
RESULTS: The overall CD rate significantly increased by 80.2% from 10.6% in 1997 to 19.1% in 2006. The greatest increase of 265% was in the Northern region and the least of 32.8% was in the Royal Commission Hospitals. Both vaginal breech and operative vaginal deliveries showed a significant decrease of 38% and 29%, respectively. There was a significant negative correlation between the increasing CD rate and the decreasing vaginal breech and operative vaginal deliveries rates. The volume of annual deliveries did not influence the CD rate.
CONCLUSIONS: A significant increase of more than 80% in the CD rate was observed from 1997 to 2006. A national strategy to reduce the CD rate is needed and will require upgrading of the existing vital registration system. We also recommend that current national data capturing mechanisms be expanded to include private sector data and to include indications for CD.

Cesarean delivery (CD) is one of the most commonly performed surgical procedures in Saudi Arabia. As reported by the Ministry Of Health (MOH) in 2006, there were a total of 784 145 surgical procedures in all government and private hospitals, of which 86 197 were CDs (11%).[1] Indications for CD range from well-defined medical indications to less-defined indications. In 1985, the World Health Organization suggested that CD should not exceed 15% of the total deliveries.[2] Globally, there is an alarming increase in the CD rate. In developed countries the rate went from about 2.5% to 6% in the 1970s to about 12% to 22% in the late 1990s.[3] In 2004, the rate in the United States reached 29.1%.[4] Data on CD rates in developing countries are not as easily available. A recent estimate of the overall rates in developing countries is 12% based on nationally representative data from 82 countries.[5] Annual increases in the rates of CD has been reported for some developing countries, ranging from 5% to 11%.[6]

The increase in CD rate is of concern not only because of the associated higher morbidity and mortality compared to the vaginal route, but also for the effects on subsequent pregnancies and deliveries. A World Health Organization global survey on maternal and perinatal health in Latin America, encompassing 120 facilities in 8 countries, looked at both maternal and perinatal outcome in relation to CD cesarean delivery. Even after adjustment for demographic characteristics, risk factors, general medical and pregnancy-associated complications, type and complexity of institution and proportion of referrals, there was a significant increase in severe maternal morbidity, such as postpartum hemorrhage, admission to intensive care units and hospital stay of more than 7 days. There was also a significant increase in maternal mortality. For perinatal outcome, there was a significant increase in length of stay to neonatal intensive care of more than 7 days.[7] The MOH in Saudi Arabia annual mortality report of 2003 revealed that among a total of 37 maternal deaths, the cause of death was related to CD in three of those deaths (8%).[8] In a cohort of 25 000 women in Scotland, the likelihood of further pregnancy following CD was significantly reduced in comparison to vaginal delivery in the index pregnancy with an adjusted odds ratio of 0.89 (95% CI, 0.82-0.96).[9] The risk of placental abruption and placenta previa in subsequent pregnancy after a first birth by CD was reported to significantly increase by 30% and 40%, respectively, compared to first birth by the vaginal route.[10] A relatively large population-based study of 12 944 women from England reported a 27-fold increase in the risk of CD among women who had previous CD section compared to those who had not.[11] The aim of this study was to review available data on the rate of CD and its determinants in Saudi Arabia.

METHODS

The main national source for CD data is the MOH. Material for this study was obtained from the Health Statistics Yearly Books covering a ten-year period from the years 1418 AH to the most recently published report for the year 1427 AH, corresponding roughly to 1997 to 2006 AD.[1,12-20] MOH yearly statistical books report maternity data in a series of tables with running totals in two categories, representing MOH hospitals and other governmental hospitals. MOH hospitals data are reported for each of the 14 administrative regions of the country (Riyadh, Makkah, Medinah, Qaseem, Eastern, Aseer, Tabouk, Ha`il, Northern, Jazan, Najran, Al-Bahah, Al-Jouf, Al-Qurayyat). Other governmental hospitals include King Khalid University Hospital, Riyadh; King Abdulaziz University Hospital, Jeddah, King Fahad University Hospital, Khobar, Armed Forces Medical Services Hospitals (all regions), National Guard Health Affairs Hospitals (all regions), Security Forces Hospital (Riyadh only), King Faisal Specialist Hospital, Riyadh;, Royal Commission Hospitals (all regions) and ARAMCO Hospitals (all regions). Unfortunately, no private hospital data are reported. Each of the 14 administrative regions and each of the other nine governmental groups of hospitals hereafter are referred to as reporting units in this study.

MOH yearly statistical books report maternity data as total number of deliveries, total number of normal deliveries and total number of abnormal deliveries. The abnormal deliveries are broken down into ventouse deliveries, forceps deliveries, vaginal breech deliveries, cesarean deliveries and others. Indications for CD are not reported. Although stillbirth and early neonatal death data are reported, yet there was a lot of missing data from multiple reporting units for these parameters, especially neonatal death. Therefore, no attempt was made to calculate perinatal mortality rates. Relevant data were extracted from the statistical yearly books (1997-2006) for each reporting unit into a computer dataset. This dataset was used to calculate yearly CD, operative vaginal delivery and vaginal breech delivery rates. To explore the effect of the volume of deliveries on the CD rate, reporting units were arbitrarily classified into low (less than 7500 deliveries per year, 11 units), intermediate (7500-15 000 deliveries per year, 4 units) and high (more than 15 000 deliveries per year, 8 units) volumes using figures for the year 2006. Descriptive and univariate analysis was performed using SPSS for Windows, version 15 (SPSS Inc., Chicago, Illinois). The Chi-square test was utilized for proportion comparisons, the Pearson correlation for assessing relationships and analysis of variance (ANOVA) for comparisons of group means. A P value of less than .05 was considered significant.

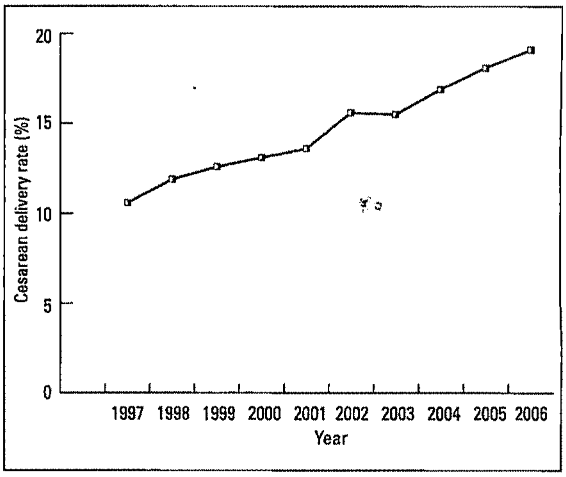


Figure 1. Trend of overall cesarean delivery rate (1997-2006).

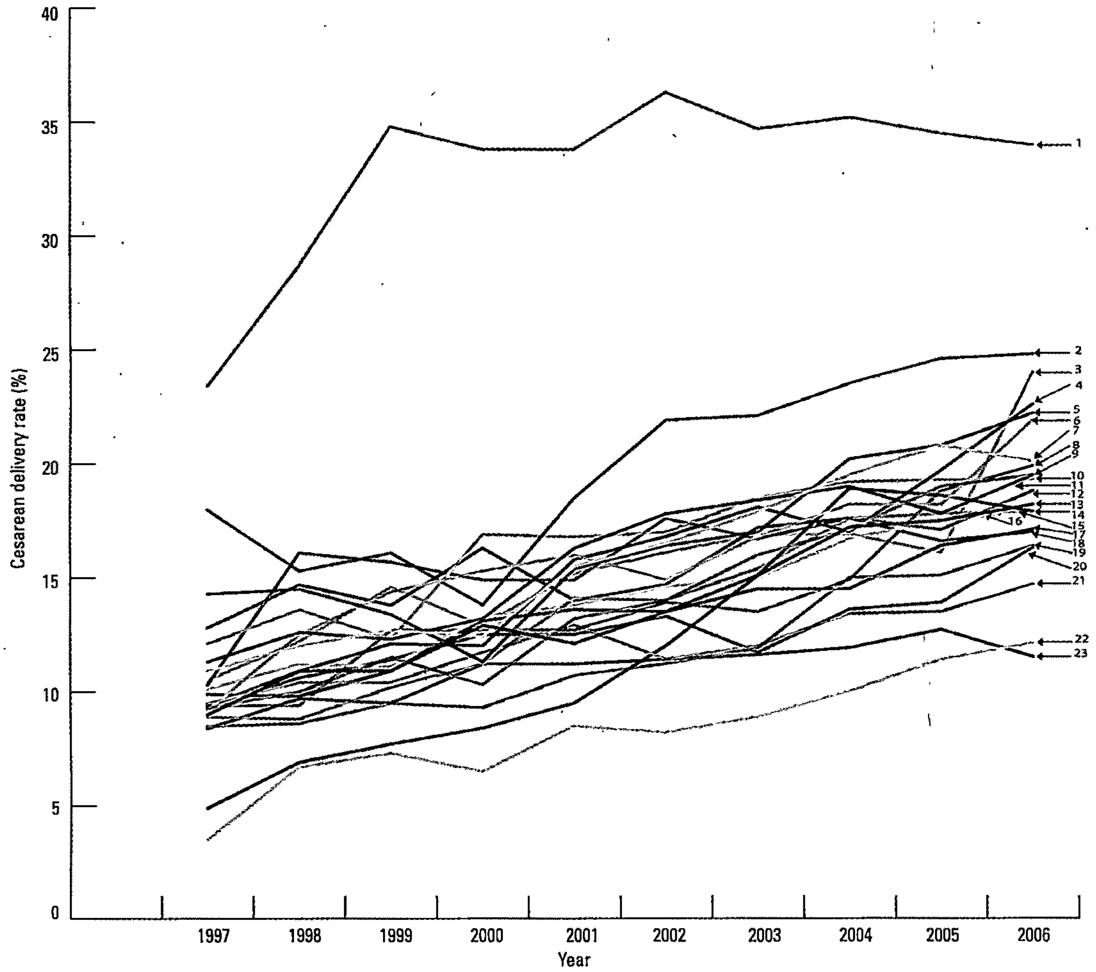
RESULTS

The overall CD rate increased from 10.6% in 1997 to 19.1% in 2006 corresponding to an 80.2% overall increase (P<.0001). Figure 1 shows the trend in CD rate over the reporting period. All the reporting units showed a progressive increase in the CD rate throughout the reporting period (Figure 2). The amount of change in the increase in CD rate between 1997 and 2006 was quite variable among the reporting units. The percentage increase in rate was highest in the northern region (265%) and was lowest in the Royal Commission Hospitals (32.8%).

The vaginal breech delivery rate significantly dropped by 38% from 2.1% in 1997 to 1.3% in 2006 (P<.0001). The decrease in vaginal breech deliveries was observed across all the reporting units. The decrease in the rate of vaginal breech delivery was quite variable among reporting units. The highest decrease was observed in the

Aseer region (94%) and was lowest in King Abdulaziz University Hospital in Jeddah (3%). Similarly, the rate of operative vaginal deliveries showed an overall significant 29% drop from 3.1% in 1997 to 2.2% in 2006 ($P<.0001$). Nineteen reporting units showed a decrease in operative vaginal delivery rate with the highest decrease in King Abdulaziz University Hospital in Jeddah (68.8%) and the lowest in the northern region (3%). Four reporting units showed an increase in the operative vaginal deliveries rate as follows: King Khalid University Hospital in Riyadh by 17.8%, Eastern region by 12.3%, National Guards Hospitals by 8.1% and Security Forces Hospital in Riyadh by 1.5%. There was a significant negative correlation between CD rates and vaginal breech delivery rates ($r=-0.94$, $P<.0001$). Similarly, there was a significant overall negative correlation between CD rates and operative vaginal delivery rates ($r=-0.89$, $P=.0006$).

The total deliveries for the year 2006, whether high (more than 15 000 deliveries per year, 8 units), intermediate (7500-15 000 deliveries per year, 4 units) or low (less than 7500 deliveries per year, 11 units) did not seem to be related to the CD rate as shown in a box and whisker plot (Figure 3). The median CD rates for the high, intermediate and low were 18.8%, 20.9% and 17.9%, respectively, while the means were 18.1%, 20.7% and 18.9%, respectively. Analysis of variance revealed that the differences in the means were not statistically



[1]King Faisal Specialist Hospital, Riyadh, [2]Ha'il, [3]Qaseem, [4]Royal Commission Hospitals, [5]King Khaled University Hospital, Riyadh, [6]Aseer, [7]Makkah, [8]ARAMCO Hospitals, [9]King Abdulaziz University Hospital, Jeddah, [10]Armed Forces Medical Services, [11]King Faisal University Hospital, Al-Khobar, [12]Eastern, [13]Al-Bahah, [14]National Guard Hospitals, [15]Security Forces Hospital, [16]Medinah, [17]Tabouk, [18]Riyadh, [19]Al-Jouf, [20]Najran, [21]Qurayyat, [22]Northern, [23]Jazan

Figure 2. Cesarean delivery rate for each of the 23 reporting units (1997-2006).

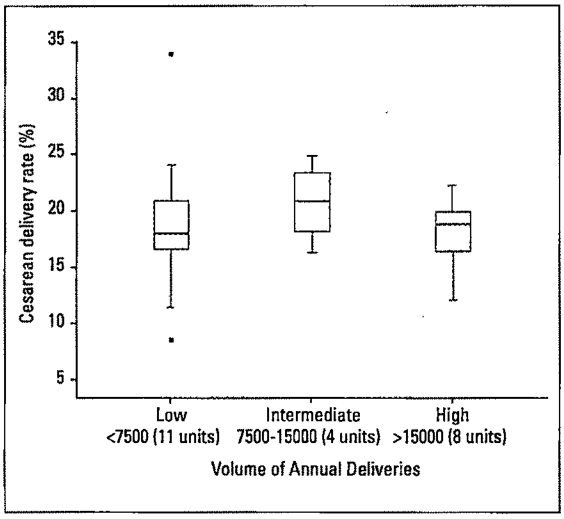


Figure 3. A box and whisker plot for cesarean delivery rates by high, intermediate and low annual deliveries units, for the year 2006. The central "box" represents the distance between the first and third quartiles with the median CD rate between them marked with a horizontal line. The lower end of the line below the central box "a whisker" represents the minimum CD rate, while the upper end of the other line above the box "another whisker" represents the maximum CD rate. Outlying values are shown as dots above or below the whiskers. There were no outliers for intermediate and high delivery volumes. There is an obvious overlap of the boxes and whiskers.

significant (P=.714). Even when the outliers were excluded the median CD rate, which is less affected by outliers, did not change, as expected, being 18.8%, 20.9% and 17.9%, respectively. The mean CD rate also changed very little, being 18.1%, 20.7% and 18.4%, respectively (P=.435).

DISCUSSION

The results of this analysis of available data shows that over the period 1997 to 2006 the CD rate went from 10.6% to 19.1%, a dramatic 80.2% increase. Although data on private hospitals were not available, it is reasonable to assume that the rate of CD in the private sector would have mirrored the rate in the public sector. Some units had higher CD rates than others (King Faisal Specialist Hospital, Riyadh and Ha'il). The available data do not provide an explanation for these higher rates, which may have been due to better reporting or a different case mix. Globally, CD rates have witnessed an alarming increase over the last few years. A recent analysis of global, regional and national estimates of births by CD revealed the following means and ranges: for the World as a whole 15% (0.4-40.5%), Africa 3.5% (0.4-15.4%), Western Asia 11.7% (1.5-23.3%), Europe 19.0% (6.2-36.0%), Latin America and the Caribbean 29.2% (1.7-39.1%), North America 24.3% (22.5-24.4%) and Oceania 14.9% (4.7-21.9%).[21] In Jordan, a report from seven military hospitals across the country revealed a rate increase from 8% for 1990-1992 to 10.9% for the 1999-2001 time periods.[22] Another report from Jordan using data from three demographic and health surveys showed that CD increased consistently, from 8.5% in 1990, to 12.9% in 1997, to 17.8% in 2002.[23] In Egypt data from the 1992, 1995 and 2000 demographic and health surveys revealed a 130% increase in rate from 4.6% in 1992 to 10.3% in 2000.[24] A CD rate as high as 26.4% was reported from nine hospitals in Beirut, Lebanon.[25] Regionally, like most developing countries, most reported CD rates reflect institutional rather than national rates. These variable sources of CD rate data coupled with a lack of national vital registration systems in most of the developing countries make meaningful in-between countries comparison unattainable.

Determinants of birth by CD include maternal age, parity, previous CD, breech presentation, multiple gestations, prolonged pregnancy and whether labor was spontaneous or induced.[3] The volume of deliveries in a reporting unit or region has also been reported to influence the CD rate.[4] Unfortunately, the available national data in Saudi Arabia do not report many of theses determinants. The available data allowed some insight into the influence of rates of vaginal breech deliveries, operative vaginal deliveries and volume of deliveries per reporting unit. The decrease in the vaginal breech deliveries across all reporting units was expected, especially after the publication of the Term Breech Trial (TBT).[26] The TBT was a randomized controlled multicenter trial comparing planned CD with planned vaginal delivery of 2083 singleton fetuses in frank or complete breech presentation at 37 or more weeks of gestation. The findings suggested that planned CD reduces adverse perinatal outcomes. Of interest is the finding that the Aseer region showed the highest decrease in vaginal breech deliveries (94%). A study from Abha (in the Aseer region) maternity hospital comparing the outcome of breech delivery at term in women before and after the TBT recommendation reported a significant increase in the rate of CDs in the years following the TBT recommendation.[27] The finding of a significant negative correlation between operative vaginal deliveries rates and CDs rates is in keeping with other studies.[28,29] In contrast to Clark et al[4] the difference in the volume of deliveries in the studied reporting units did not influence the CD rate in the current study.

The rise in the CD rate is alarming. Given the associated morbidity and mortality, it is imperative that a national strategy be considered to reduce at least some of the unnecessary CDs. The limitations and inadequacies of the current national data set preclude the development of any national strategy. It is recommended that the current national data capturing mechanisms be upgraded in terms of coverage of determinants of CD and sectors. Important parameters are missing from the current capturing tools such as indications for CD caesarean delivery. This will entail paying attention to operational definitions of the determinants, validity and reliability of the captured data, analysis and presentation for policy modification and trending analysis. Any attempt at tackling the increasing CD rate has to be data driven. Evidence-based strategies to reduce CD rates have been reported.[30,31] Given the many possible reasons for deciding on CD, interventions to reduce CD rates are by necessity multifaceted. Evidence-based strategies that have shown an impact on CD rate include behavioural modification of providers, active management of labor, offering a trial of scar to women with previous CD cesarean delivery, external cephalic version for breech presentation at term, and routine induction for uncomplicated pregnancies at 41 weeks.

Possible reasons of the increase in the CD rate include improvements in the health care system in Saudi Arabia, a rising primary CD rate, provider perception of the safety of the procedure and defensive practices. However, all of these reasons are speculative.

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Oral sucrose and a pacifier for pain relief during simple procedures in preterm infants: a randomized controlled trial

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Ann Saudi Med 2009; 29(3): 184-188

BACKGROUND AND OBJECTIVES: Previous randomized trials of the analgesic effects of sucrose, glucose, and a pacifier in term neonates have shown that the pacifier resulted in lower pain scores than glucose or sucrose, but the pacifier with and without sucrose did not differ. The current study was designed to assess the analgesic effect of pharmacologic (sucrose, water) and a non-pharmacologic measures (pacifier) in preterm infants and to find whether there is any synergism between these intervention in relieving pain during painful procedures.

PATIENTS AND METHODS: In this double-blind, randomized, controlled study, 36 preterm infants (mean 31 weeks gestational age, range 27 to 36 weeks) were randomly allocated to six different regimens (0.5 mL sterile water with pacifier, 0.5 mL sterile water without pacifier, 0.5 mL sucrose 24% with pacifier, 0.5 mL sucrose 24% without pacifier, pacifier alone and control group) during a stay in intensive care of up to 15 days. Pain scores were measured with the Premature Infant Pain Profile (PIPP), a validated behavioral acute pain scale.

RESULTS: Of all the regimens, the lowest pain scores occurred with the use of 24% sucrose solution combined with pacifier. The mean pain score for the combination of sucrose with pacifier was 0.7 as compared to 1.4 for the sterile water with pacifier group ($P<.05$).

CONCLUSION: The synergistic effect of the combination of sucrose and non-nutritive sucking was clinically effective and safe in relieving the pain of simple procedures such as venipuncture or heel stick in preterm and term infants, but further research is needed on these interventions alone and in combination with other behavioral interventions in neonates.

Treating pain in the newborn is essential for many reasons, both clinical and ethical. Pain can lead to decreased oxygenation, hemodynamic instability, and increased intracranial pressure.[1] For neonates receiving intensive care, it is widely accepted that central analgesics, administered intravenously, should be used to relieve pain.[1] However, infants who are less sick or who are not in neonatal intensive care units usually do not receive an analgesic for painful procedures. Obviously, central analgesics cannot be used for pain associated with occasional blood sampling performed in newborns not in intensive care. It is therefore essential to find simple, acceptable, and well-tolerated methods to reduce pain in these infants.[1] Non-nutritive sucking during heel prick procedures decreases behavioral distress in the newborn infant.[2] Studies support the theory that sucrose (due to the sweet taste) and pain relief are interrelated through the body's endogenous opioid system which provides natural analgesia.[3-9] The analgesic effect of sucrose is reversed with administration of naloxone, an opioid antagonist, suggesting that sucrose activates the central endogenous opioid system, with an action similar to that of opioid analgesics.[10,11] Our objective was to assess and compare the analgesic effects of sucrose versus sterile water alone or with a pacifier in relieving pain in preterm infants prior to painful procedures. We also sought to determine whether there is a synergistic effect with oral sucrose when combined with non-pharmacologic interventions to relieve pain during painful procedures in preterm infants.

PATIENTS AND METHODS

This was a randomized, prospective, double-blinded, controlled study of the analgesic effects of sucrose versus sterile water alone or with a pacifier in preterm infants admitted to the neonatal intensive care unit (NICU) of a tertiary care hospital. The study protocol and consent form were approved by the hospital institutional review board. Recruitment was done between January 2005 and May 2007. The inclusion criteria were that subjects had to be preterm infants of less than 37 weeks of gestational age admitted to the NICU at King Faisal Specialist Hospital, Jeddah. There had to be a signed parental consent prior to enrollment. Exclusion criteria were: 1) exposure antenatally to maternal sedation (opioid); 2) occurrence of any procedure performed within 24 hours in preterm infants whose mothers had had general anesthesia during delivery; 3) the presence of major neurologic abnormalities; 4) Apgar scores at 5 minutes of <5; 5) presence of necrotizing intestinal colitis; 6) nothing by mouth status for any reason and 7) being preterm with hyperglycemia.

Of 48 preterm infants of <37 weeks gestational age admitted and expected to be included in this study, 36 infants (72%) completed the study. The other 12 infants were eligible but they did not complete the study because of failure to get parental consent. Every patient participating in the study received each of six different regimens during a maximum stay of 15 days from admission or the end of the NICU stay (whichever came first). The solutions were prepared and coded in the pharmacy and none of the investigators or family of the patient knew the identity of the solution. Documentation of the identity of the solution was kept in a closed cabinet that was opened only at the time of analyzing the results. The nurse opened a consecutively numbered envelope (all envelopes were previously prepared with codes for the six treatment regimens, each in a folded paper). For each assignment, a paper was randomly picked so that assignments were random and double-blinded for the sucrose and water solutions. The six regimens were 0.5 mL sterile water with pacifier, 0.5 mL sterile water without pacifier, 0.5 mL sucrose 24% with pacifier, 0.5 mL sucrose 24% without pacifier, pacifier alone (standard nipple stuffed with gauze square for resistance, held in the infant's mouth for 2 minutes prior the procedure and kept gently in the infant's mouth throughout the procedure), and standard of care or no treatment (control group). For the sucrose and water solutions, the tip of a 1 mL syringe without the needle was placed in the infant's mouth and the solution was instilled with gentle movements of the syringe to stimulate sucking for 30 seconds. Each treatment was given 2 minutes prior to the procedure.

The primary outcome measure was the evaluation of pain induced by venipuncture using the Premature Infant Pain Profile (PIPP). Using this scale, the neonate is observed for 15 seconds and the following seven indicators are scored: gestational age, behavioral state, heart rate increase from baseline, oxygen saturation change from baseline and duration of time that the infants have brow bulge, eye squeeze and a naso-labial furrow (Figure 1).[12] Heart rate was measured by pulse oximetry, and considered only when the quality of the registered wave was adequate. Bradycardia was defined by a heart rate less than 80 beats per minute and tachycardia by a heart rate above 160 beats per minute. Oxygen saturation was evaluated by pulse oximetry, taking into account the quality of wave registered. Hypoxia was defined by an oxygen saturation below 88% (an oxygen saturation 15% less than the patient's baseline was used in patients with cyanotic heart disease). The physiologic and behavioral

Points	FINDING	INDICATOR
0	☐ Quiet, no facial movement ☐ Heart rate stable ☐ No desaturation ☐ No brow bulge ☐ No eye squeeze ☐ No nasolabial furrow	
1	☐ Quiet, no facial movement ☐ 5-14 beats per minute increase in heart rate ☐ Slight desaturation ☐ Minimum brow bulge ☐ Minimum eye squeeze ☐ Minimum nasolabial furrow	
2	☐ Active, some facial movements ☐ 15-24 beats per minute increase in heart rate ☐ Moderate desaturation ☐ Moderate brow bulge ☐ Moderate eye squeeze ☐ Moderate nasolabial furrrow	
3	☐ Active/awake, eyes open, facial movements ☐ ≥ 25 beats per minute increase in heart rate ☐ Severe desaturation ☐ Maximum brow bulge ☐ Maximum eye squeeze ☐ Maximum nasolabial furrow	

Brow bulge, eye squeeze, nasolabial furrow: none (≤ 9% of time), minimum (10-39% of time), moderate (40-69% of time), maximum (≥ 70% of time).

Oxygen saturation minimum: no desaturation (0 to 2.4% decrease), slight desaturation (2.5 to 4.9% decrease) moderate desaturation (5.0 to 7.4% decrease), severe desaturation (7.5% decrease or more).

Heart rate maximum: stable heart rate (0-4 beats per minute increase), minimum increase (5-14 beats per minute increase), moderate increase (15-24 beats per minute increase), maximum increase (≥ 25 beats per minute increase).

Interpretation: Minimum score: 0, Maximum score: 3

Figure 1. The Premature Infant Pain Profile (PIPP) pain evaluation tool.[12]

pain parameters were evaluated at six different times: immediately prior the procedure, during venipuncture, one minute after the procedure, three minutes after the procedure, five minutes after the procedure, and ten minutes after the procedure. The response time (crying time) was assessed at 0, 1, 3, 5, and 10 minutes.

Repeated measures analysis of variance was used for the statistical analysis. Pain score comparisons between different treatments were summarized using mixed between-within ANOVA. Results were significant when P<.05. Because the F statistic is based on the ratio of between-group variance to within-group variance, there must be a very large between-group difference to attain a significant result; that is, the large variability among the subjects could obscure any real differences between the groups. This is especially true if the groups are small. One way to remove these individual differences is to assign each subject to all treatments with each subject exposed to medications 1 through 5 and the control in random order. Each subject serves as their own control, and the within or error variance is decreased. This results in a more powerful test and decreases the number of subjects needed for the study.[13] The pre-procedure pain score means ranged from 0.037 to 0.15 in all groups so these scores were not included in further analysis due to the small values. Further analysis was done for the five treatment times (0, 1, 3, 5, and 10 minutes).

Table 1. Demographic and clinical characteristics of 36 preterm babies.

	Median (range)	Mean (SD)
Apgar score	8.5 (8-10)	8.6 (0.6)
Body weight (kg)	1.7 (0.6-2.5)	1.7 (0.6)
Gestational age (weeks)	32 (27-36)	32.4 (2.9)

RESULTS

Demographic and clinical characteristics of the 36 preterm infants are shown in Table 1 . There were no significant differences between treatment groups in heart rate, blood pressure, O_2 saturation and glucose measurement (P>.05) (Table 2), but there were significant differences in crying time and pain score (P=.001). Pain scores were hghest at 1 minute past painful stimuli for all five treatment groups (Figure 2). The use of 24% sucrose solution combined with pacifier resulted in the lowest pain score of all groups for all measurements from zero to ten minutes (P<.05). In all treatment groups, the lowest pain-scores were pretreatment scores with the means ranging from 0.037 to 0.15. Pain scores elevated gradually at zero-time (range, 0.69 to 1.69) and elevated even further at 1 minute to reach a peak (range, 1.077 to 2.52). At 3 minutes they dropped (range, 0.85 to 2.1) and dropped further at 5 minutes (range, 0.38 to 1.5) There was a change in pain scores over the five time periods (main effect for time) and this change was statistically significant (Wilks lambda=0.145, F=214.6, P<.0005, multivariate partial eta squared =0.855). There was also a statistically significant difference in pain scores between treatment groups [F (5, 149)=14.75, P=.0005] and the change in pain scores over time was different for the treatment groups with an interaction effect (Wilks lambda=0.63, F=3.56, P<.0005).

DISCUSSION

In ths study, oral sucrose administration before an acute painful procedure decreased the behavioral pain indicators and composite pain scores in neonates undergoing heel stick and/or venipuncture as measured by the PIPP. The pain score was significantly reduced in infants who

Table 2. The mean values for Premature Infant Pain Profile measurements during the six different treatments.

	Sterile water + pacifier	Sterile water	Sucrose 24% + pacifier	Sucrose 24%	Pacifier alone	Control	*P*
Heart rate (beats/min)	160.5	161.8	155.3	156.9	162.2	163.1	.167
O_2 saturation (%)	90.9	91.3	91.4	91.2	90.6	91.5	.979
Respiratory rate (breaths/min)	50.8	54.4	48.2	46.3	48.8	50.3	.193
Crying time (s)	11.3	11.5	4.6	6.1	11.8	17.4	.001
Blood pressure(mm Hg)	50.2	48.9	45.4	48	46.9	46.7	.246
Glucocheck (mmol/L)	4.5	4.8	5.5	5.1	4.7	4.9	.227

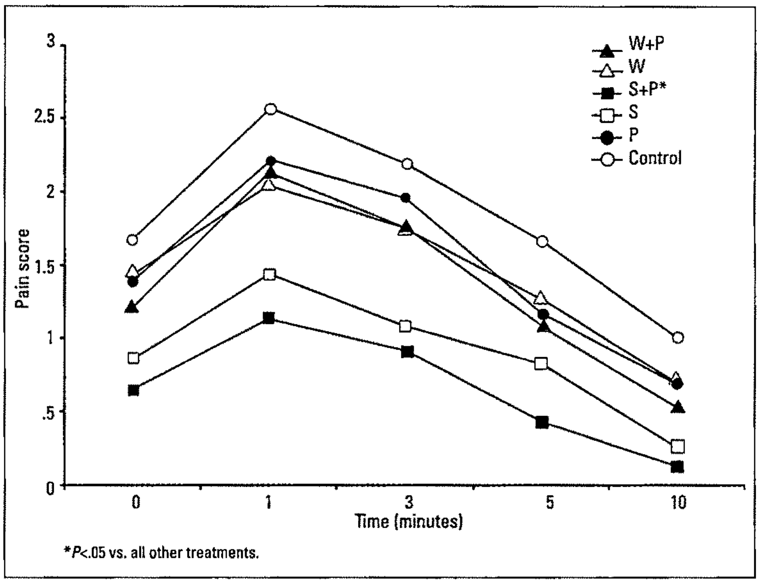
Values are means.

received 0.5 mL (0.12 gm) of 24% sucrose solution with mean pain score of 0.9 at the 0.05 level of significance. The combination of pacifier and sucrose 24% solution showed more clinical effect and reduced the mean crying time to 4.6 seconds (Table 2) which was statistically significant (P=.001).

Similar results were described in previous studies where sucrose was found to be safe and effective in newborn infants for reducing procedural pain from single painful events such as heel lance or venipuncture.[14,15] Sucrose provided an additional benefit when used with a pacifier in infants aged 1-3 months undergoing venipuncture in a pediatric emergency department.[16] A modest 16% reduction in overall pain among newborns of both diabetic and nondiabetic mothers was reported when sucrose was used repeatedly for all procedures performed in the first two days after birth, but when each procedure was evaluated separately, the effectiveness of sucrose was limited to venipuncture.[17]

The use of sterile water alone or pacifier alone or the combination of sterile water and pacifier during painful stimuli were not statistically different in their effect on pain relief and were not better than the control group that received the standard of care or no pain control for simple procedures. The mean pain score was 1.4, 1.4, 1.5 and 1.8 respectively. However, one review recently concluded that the overall effects of non-nutritive sucking on pain related to minor procedures were generally superior to standard care.[18] Reports included in this review found that relative to standard care, non-nutritive sucking resulted in reduced crying behavior, reduced heart rate and lower behavioral distress. However, several methodological problems were also noted in this review as the authors of these reports evaluated crying behaviors using a subjective, unvalidated scale.[2,19,20]

Arranging all the treatment groups in our study with respect to the mean pain score showed that the highest pain score occurred at one minute post-painful stimuli with all the treatment groups, but the maximum pain occured with the control group or with the use of the pacifier alone for pain relief with a pain score of 2.5 and 2.2, respectively. The lowest pain score occurred at 10 minutes with a mean pain score of 0.1, 0.3, 0.5, 0.7, 0.7 and 1 with the use of sucrose 24% combined with pacifier, sucrose 24% solution, sterile water combined with pacifier, sterile water alone, pacifier alone and control group respectively. In preterm infants, it has also been reported that the provision of sucrose and a pacifier is more effective than sucrose alone in reducing procedural pain as measured by the PIPP score in three reports.[9,21,22]



*P<.05 vs. all other treatments.

Figure 2. Pain scores for treatment regimens (P: pacifier, S: sucrose 24%, W: sterile water).

It is important to emphasize that using 24% sucrose has no side effects and is safe for preterm analgesia. This is supported by evidence reported in the literature where sucrose was a useful and safe analgesic for minor procedures in neonates given 2 mL of 25% sucrose solution before venipuncture, which significantly reduced crying time.[23] Currently the standard practice during venipuncture in newborn infants is not to use any analgesia. This study demonstrated the ease of use of sucrose and/or pacifier use, which should inspire a change in practice toward the use of routine sucrose analgesia during the first weeks of life in preterm infants. This practice is supported by published guidelines for pain relief using sucrose analgesia during minor procedures such as heel stick or venipuncture. These guidelines state that dipping the pacifier in 24% sucrose solution or using oral syringe application directly on the tongue, each dip >0.2 mL applied 1 to 2 minutes before or during painful procedure. Sucrose administration can be repeated as needed for pain relief.[24]

The synergistic effect of the combination of sucrose and non-nutritive sucking is a statistically and clinically effective and safe intervention for relieving pain during simple procedures as venipuncture or heel stick in preterm and term infants. Additional research is needed on the efficacy and safety of implementing these interventions, alone and in combination with other behavioral interventions (e.g. facilitated tucking, kangaroo care) in neonates. In addition, research is needed on the influence of implementing these interventions on pain response and clinical outcomes in very low birth weight neonates in the NICU.

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original article

Extra-articular manifestations of rheumatoid arthritis: a hospital-based study

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Accepted for publication March 2009

Ann Saudi Med 2009; 29(3): 189-193

BACKGROUND AND OBJECTIVE: The frequency of extra-articular manifestations in rheumatoid arthritis (ExRA) differs from one country to another, so we investigated ExRA frequency in a well-defined hospital patient population with rheumatoid arthritis (RA) in Saudi Arabia. We also examined possible predictors of the development ExRA.

METHODS: A retrospective analysis was conducted of all patients diagnosed with RA at a university hospital during a 4-year period. Cases were classified according to the 1987 American College of Rheumatology criteria for RA, and the frequency of ExRA was recorded.

RESULTS: Of 140 patients who fulfilled the criteria for the diagnosis of RA, 98 (70%) developed ExRA features. Anemia occurred in 61%, thrombocytosis in 16%, pulmonary involvement in 10%, and renal amyloidosis, vasculitis and Felty syndrome were present in 6%, 2% and 1%, respectively. The mortality rate was high (16%) in patients with ExRA. The predictors for mortality were lung involvement, age over 50 years and kidney amyloidosis.

CONCLUSION: ExRA were present in a substantial proportion of our patients, which lead to a worse disease outcome. Anemia, thrombocytosis and respiratory system involvement were the commonest. Early recognition and treatment are important to decrease mortality.

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammatory polyarthritis and systemic features, with a prevalence of 1% in Western populations.[1] In one study in Saudi Arabia, the prevalence was 0.02% in the Al-Qassem region.[2] Extra-articular manifestations of rheumatoid arthritis (ExRA) occur in about 40% of patients, either in the beginning or during the course of their disease.[3] The presence of ExRA is associated with severe active disease and increased mortality compared to the general population.[4,5]

The frequency of ExRA specific manifestations is highly variable because of case definitions and study design. For example, nodules are easily identifiable and their incidence was reported as 30%, while pulmonary fibrosis is not clinically apparent and has a reported incidence in population studies of 6.1% compared with 30% in case findings.[6] Using previously applied definitions for ExRA is of major importance to unify the diagnosis.[7,8]

There are no reliable predictors for the development of ExRA, although many have been suggested.[7-9] They include such constitutional factors as male sex, association with HLA-related shared epitope genes, autoantibodies such as rheumatoid factor (RF), antinuclear antibodies (ANA) and anti-cyclic citrullinated peptide antibody (anti-CCP), as well as environmental factors such as smoking.[10-15] Due to the systemic inflammatory process, the incidence of mortality in RA is increased by four-fold compared with the general population.[16] Although few patients die of the disease, or of specific complications such as cervical instability or drug side effects, the major factors that predict mortality are the presence of co-existing heart and lung disease, malignancy and dementia.[17] Other suggested factors that predict mortality are active disease despite medical treatment and the presence of ExRA.[18] In this study, we reviewed the incidence of ExRA retrospectively at a university hospital in Jeddah, Saudi Arabia, and identified clinical and biochemical risk factors for developing ExRA.

METHODS

This retrospective study was conducted at King Abdulaziz University Hospital, the only teaching governmental hospital in Jeddah. The facility provides health care to a multinational population of mixed socioeconomic status. A computerized retrieval system was used to identify all patients with a registered diagnosis of RA who received treatment at the hospital during a 4-year period (1 January 2004 to 30 December 2007). RA patients were identified according to the 1987 American College of Rheumatology classification criteria for RA (the most current criteria for RA diagnosis).[19] The data collected from records included demographic features, clinical findings, including duration of the disease at the time of the study (classified as <1 year, ≥1 to 5 years, and >5 to 10 years, and >10 years), disease activity (based on the number of tender/swollen joints or the disease activity score obtained from the 28-joint count),[20] treatment, the presence of articular and extra-articular manifestations of RA, a positive family history of RA and associated co-morbidities, laboratory parameters (complete blood count, rheumatoid factor [RF] and antinuclear antibody [ANA]), and radiological changes (characteristics of lesions on chest radiographs and the typical radiological features of involved joints).

Extraarticular features included renal invovlement defined as urinary excretion of more than 500 mg protein/24 hours, cellular casts not attributable to infection, or abnormal histology on renal biopsy. Amyloidosis was considered if confirmed by biopsy or fine needle aspiration. Respiratory involvement was defined as pleuritis or interstitial lung disease, scarring and the formation of nodules in the lungs documented by a high-resolution CT scan of the chest. Pericardial involvement was considered if pericarditis and/or pericardial effusion was documented in the clinical record as related to RA. Nervous system involvement was considered compression neuropathy (e.g. carpal tunnel syndrome) and peripheral neuropathy. Sjogren syndrome was defined by dryness of the eyes (xerophthalmia) and mucous membrane (xerostomia). Rheumatoid nodules were defined as subcutaneous nodules with a diameter ≥5 mm in the extensor surfaces of the extremities and fingers. Hematological changes included leucopenia (WBC count $<4\times10^9$/L), thrombocytosis (platelet count $>400\times10^9$/L), anemia (normochromic, hypochromic or megaloblastic). Felty syndrome was considered present if there were neutropenia plus splenomegaly documented by ultrasound in the absence of other causes in the RA patient. Rheumatoid vasculitis was defined as the presence of mononeuritis multiplex or acute peripheral neuropathy, peripheral gangrene, histological evidence of necrotizing arteritis, or deep cutaneous ulcers. Ischemic heart disease, lung disease, infection and malignancy were considered co-morbid illnesses. Gender, duration of the disease, RF, ANA and smoking (either active or had stopped within the last 5 years) were evaluated as risk factors for the development of ExRA. We examined the effect of age, gender, RF and the presence of co-morbid illness on the mortality rate in patients with ExRA.

Data analysis was done using Statistical Package for Social Sciences (SPSS software, version 11). Mean and standard deviation were calculated for quantitative data and proportions for categorical variables. One-Way ANOVA and the t test were used for comparing means of continuous variables. Proportions were compared by the chi-square test and the Mantel-Haenszel test as required. Results were considered significant if the *P* value was less than .05. Multivariate logistic analysis was used to evaluate possible predictors of mortality.

RESULTS

One hundred ninety-two patients were diagnosed as having RA. Fifty-two were excluded due to incorrect diagnosis (such as registration error, premature diagnosis, or the case records did not contain enough data to support the diagnosis). One hundred forty fulfilled the 1987 American College of Rheumatology classification criteria for the diagnosis of RA. A total of 98 of 140 (70%) had features of ExRA.

Seventy-four patients (75%) were women while 24 (25%) were men. Their mean (SD) age at the time of the study was 47.2 (15.6) years for females and 44.6 (13.2) for males. Sixty-one percent patients (62%) were Saudi. Duration of the disease at the time of the study is illustrated in Table 1. Three percent of our patients were smokers. Only two patients had a family history positive for RA. The main extra-articular features are shown in Table 2. Anemia was found in 60 patients (61%). Iron deficiency anemia was the commonest, affecting 52 of 60 anemic patients (87%). Normochromic normocytic anemia affected 8 patients (13%). Thrombocytosis, whether considered reactive to iron deficiency anemia or as an RA activity marker was found in 16 patients (16%). Respiratory system involvement was a common feature, affecting 10 patients (10%) in the form of interstitial lung disease and pleuritis in 7 patients (7%), while leukopenia was found in only 5 patients (5%). The lymph nodes were enlarged in 4 patients (4%). Carpal tunnel syndrome and rheumatoid nodules were present in 3 patients (3%) while Sjogren syndrome and leg ulcer were present in 2 patients (2%). Pericardial effusion and Felty syndrome were the least frequent feature found in RA patients, occurring in 1 patient only (1%). Pericardial effusion was detected in 1 patient (1%). Vasculitis was found in 2 patients (2%).

RF was detected as positive in 72 patients (73%), according to our laboratory reference (set point range, 0-20 IU/L). ANA was positive in 37 (38%) patients. Only 20 patients (20%) performed a urine analysis. Proteinuria was found in 10 (10%) and 2 (2%) had RBC casts as well as proteinuria. Renal amyloidosis was observed in 6 patients (6%). Radiological changes were documented as periarticular erosions in 28 patients (29%) and atlantoaxial sublaxation in 4 patients (4%). Thirty-four patients (35%) had the disease in its active form. Fifty-three patients (54%) were receiving treatment in the form of disease-modified antirheumatic medication. Co-morbidities were observed in 25 patients (21%) (Table 3).

In RA patients with ExRA, the mortality rate was 16% (16 patients). In the multiple logistic regression analysis, there were certain predictors for mortality among our patients; respiratory system involvement was the major predictor with a significant statistical association (*P*=.001). The second predictor for mortality was the age of patients, as mortality was higher in those aged 50 years or older (*P*=.01). Kidney amyloidosis was the third significant associated factor (*P*=.05) while sex difference and RF did not show any significant association with mortality (*P*=.08, *P*=.9, respectively).

DISCUSSION

The frequency of ExRA was 70% among our patients. This is higher than in North American populations (40%), but similar to the British population (68%).[1-5] Based on our search of the literature, no previous study has evaluated the percentage of ExRA in the western region of Saudi Arabia. Anemia was the most common ExRA in our population, occurring in 61% of patients, while thrombocytosis occurred in 16%, followed by interstitial lung disease in 10%. Comparing our study to Western reports, iron deficiency anemia was much higher among our patients, which might be explained by chronic blood loss due to drug side effects or poor dietary intake of iron-rich food.[21] The prevalence of interstitial lung disease was similar to that in previous reports.[6,20] Kidney amyloidosis, found in 6% of patients, is frequently present late in the disease and is related to worse outcomes, including mortality.[18,21]

Only a small proportion of our patients (20%) had routine evaluation of their kidney function, which is a limitation of the study. The results may have differed if all patients had evaluation of their renal function. We recommend more frequent evaluation of renal involve-

Table 1. Duration of the disease at the time of first presentation.

Number of years	Number of patients (n=98) n (%)	Sex (M:F) n (%)	Mean (SD) age in years
<1 year	6 (6)	1:5 (17:83)	38 (15.3)
≥1-5 years	25 (25)	7:18 (28:72)	38.5 (15.3)
>5-10 years	29 (30)	7:22 (24:76)	49.2 (13.3)
>10 years	38 (39)	9:29 (24:76)	51.3 (13.9)

Table 2. Main extra-articular manifestations of rheumatoid arthritis.

Extra-articular manifestation	Number of patients (n=98) n (%)
Pericardial effusion	1 (1)
Felty syndrome	1 (1)
Leg ulcer	2 (2)
Sjogren syndrome	2 (2)
Rheumatoid nodules	3 (3)
Carpal tunnel syndrome	3 (3)
Lymphadenopathy	4 (4)
Amyloidosis	6 (6)
Respiratory involvement	10 (10)
Anemia	60 (61)
Normochromic normocytic	8
Iron defeciency	52
Leukopenia	5 (5)
Thrombocytosis	16 (16)

Table 3. Associated co-morbidities in rheumatoid arthritis patients.

Co-morbidity	Number of patients (n=98) n (%)
Tuberculosis	6 (6)
Hypertension	5 (5)
Diabetes	4 (4)
Malignancy	3 (3)
Coronary artery disease	3 (3)
Cerebral vascular accident	2 (2)
Thrombosis	2 (2)

ment in patients with RA, especially in patients with a prolonged disease to evaluate proteinuria and casts. Surprisingly, rheumatoid nodules, which are reported to occur in 30% of patients,[20] were only found in 3% of our population, which may have been due to underreporting of rheumatoid nodules. Other classic features (secondary Sjogren syndrome, Felty syndrome and neuropathy) were the least common, occurring in 3%, 2%, and 1% of the patients, respectively.

Our study showed that most patients who developed ExRA had positive rheumatoid factor (detected in 73% of our patients) and this was similar to previous reports.[20] Data are conflicting as to whether the occurrence of ExRA decreases with prolonged disease duration. Turesson et al demonstrated that ExRA does not decrease during a 10-year follow-up.[22] Our study showed a similar finding, as our patients reported more ExRA with prolonged disease duration (>10 years). Although smoking was suggested as a risk factor for the development of ExRA, we could not relate a significant association in our study as only 3% of our patients were active smokers.

RA is associated with a high risk for morbidity and premature death secondary to the earlier development of cardiovascular, lung diseases and malignancy.[16-18] In our patients, the overall mortality rate was observed to be high (16%), with the following predictors: respiratory system involvement (P=.0001), age older than 50 years (P=.01) and kidney amyloidosis (P=.05). When we compared males with females, sex had little effect on the disease pattern, severity, or the presence of ExRA and mortality.

Our findings may differ from those found in Western patients, which could be due to different human leukocyte antigen (HLA) associations with RA between Caucasian and other populations. RA in the Saudi population is associated with HLA DR10, while in Caucasians it was associated with HLA DR4 and HLA DR1.[23]

Because our study was retrospective, our analysis was limited to case-recorded data collected by the managing physician. On the other hand, the observations documented by the treating doctor reflected manifestations considered clinically relevant. We recommend further prospective studies to document the predictors for the development of the ExRA and outcome in our society. We recommended further research to ascertain the mortality rate in RA patients with and without ExRA and to define the individual risk factors associated with high mortality.

We have demonstrated that ExRA is present in a substantial proportion of a hospital-based sample and is generally associated with a worse disease outcome. Patients with ExRA have a high mortality rate, which could be related to the complication of the disease itself or the presence of other co-morbid illnesses. ExRA needs to be recognized and managed early to decrease the mortality rate.

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original article

Anthropometric predictors of incident type 2 diabetes mellitus in Iranian women

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Ann Saudi Med 2009; 29(3): 194-200

BACKGROUND AND OBJECTIVES: Studies have shown a strong association between excess weight and risk of incident diabetes in Iranian women. Therefore, we investigated anthropometric indices in the prediction of diabetes in Iranian women.

SUBJECTS AND METHODS: We examined 2801 females aged ≥20 years (mean [SD] age, 45.2 [12.9] years) in an Iranian urban population who were non-diabetic or had abnormal glucose tolerance at baseline. We estimated the predictive value of central obesity parameters (waist circumference [WC], waist-to-hip ratio [WHR], waist-to-height ratio [WHtR], body mass index [BMI]) in the prediction of diabetes. We classified each parameter in quartiles and compared the lowest with the highest quartile after adjusting for confounding variables, including age, hypertension, triglyceride levels, HDL-cholesterol, family history of diabetes, and abnormal glucose tolerance in a multivariate model. Receiver operator characteristic (ROC) curves were used to determine the predictive power of each variable.

RESULTS: Over a median follow up of 3.5 years (11 months-6.3 years), 114 individuals developed diabetes (4.1%). The risk for developing diabetes was significantly higher for the highest quartile of BMI, WC, WHR and WHtR, respectively, compared to the lowest quartile, and the risk decreased but remained statistically significant when abnormal glucose tolerance was included in the multivariate model. WHtR had the highest area under the ROC curve.

CONCLUSIONS: In Iranian women, BMI, WC, WHR, WHtR were predictive of development of type 2 diabetes, but WHtR was a better predictor than BMI.

Obesity, which increases the risk of coronary heart disease, stroke and type 2 diabetes mellitus (DM), is an important determinant of health.[1,2] The prevalence of obesity and overweight is increasing in developing countries, including Iran.[1,2] DM receives more attention than other related diseases both clinically and in public health.[3] A prospective epidemiological study showed that increased abdominal fat accumulation is an independent risk factor for cardiovascular disease.[4] Some studies have suggested that waist circumference (WC) is a better predictor for DM than other indicators of obesity.[5,6] Others have shown that the waist-to-hip ratio (WHR) is the best predictive anthropometric variable for development of type 2 DM.[7,8] In a recent meta-analysis, Vazquez et al showed that body mass index (BMI), WC and WHR had a similar association with incident diabetes.[9] The ability of obesity indicators to predict diabetes may differ by ethnicity, age and sex.[10,11] Our recent study in Iran showed that incident type 2 diabetes is largely attributable to being overweight, particularly in women.[12] In the Pima Indian population, BMI and waist-to-height ratio (WHtR) in men, and BMI, WC and WHtR in women were the best predictors of incident diabetes.[13] Recently, we showed that WHtR was better than BMI in identifying men at risk of diabetes.[14] This study was designed to determine the best anthropometric predictor of diabetes in a population-based study in urban Iranian women.

METHODS

This study was conducted within the framework of the Tehran Lipid and Glucose Study (TLGS), a prospective study conducted on a representative sample of residents of district 13 of Tehran (the age distribution and socioeconomic status of the population in district 13 is representative of the overall population of Tehran), with the aim of determining the prevalence of non-communicable disease risk factors and developing a healthy lifestyle to improve these risk factors.[15] In the TLGS, 15 010 people aged 3 years and older living in district 13 of Tehran were selected by a multistage cluster random-sampling method.[15] They included 10 368 subjects aged ≥20 years evaluated in the cross-sectional phase 1 of TLGS. Phase 1 was a cross-sectional prevalence study of non-communicable diseases and associated risk factors implemented from March 1999 to December 2001. Phase 2 was a prospective follow-up study which had begun from 2002 to 2005, aiming to determine the trend of non-comunicable disease risk factors and incidence in a representative population. By the end of September 2005, 6246 individuals (59% females and 41% males) had participated in phase 2 of TLGS with a median follow-up duration of 3.5 years (11 months-6.3 years). From this population, 743 with diabetes (271 subjects with current use of a hypoglycemic agent and 472 with newly diagnosed diabetes according to the oral glucose tolerance test results [OGTT]) and 448 with missing data were excluded. Subjects with other forms of glucose intolerance such as impaired GTT or impaired fasting glucose were not excluded. Thus, from 5055 non-diabetic subjects (2085 males and 2970 females) at baseline, 2801 females with full data were included in this study. The main reasons for lack of attendance at follow up examinations despite repeated calls were either immigration (30%) or personal reasons. The Ethical Committee of The Endocrine Research Center of Shahid Beheshti University of Medical Sciences approved the protocol for this study. Informed written consent was obtained from all subjects.

Subjects in each phase were interviewed privately and face-to-face by trained interviewers using pre-tested questionnaires. Initially, information on age, smoking habits, family history of diabetes, and medication use was collected. Subjects who reported a parent or sibling with diabetes were considered to have a positive family history of diabetes and those with a current or past history of smoking were designated as smokers. Weight was recorded to the nearest 100 grams while minimally clothed without shoes using digital scales. Height was measured in a standing position, without shoes, using a tape stadiometer with a minimum measurement of 1 mm, while the shoulders were in a normal state. BMI was calculated as weight in kilograms divided by height in meters squared. WC was recorded to the nearest 0.1 cm at the umbilical level and hip circumference at the maximal level over light clothing, using an unstretched tape meter, without pressure on the body surface. WHR was calculated as WC divided by hip circumference and WHtR as WC (cm) divided by height (cm). To avoid interobserver error, all measurements were taken by the same person. After the patient rested for 15 min, a qualified physician measured blood pressure, taking two measurements (one initial measurement for determining the peak inflation level) in a seated position using a standard mercury sphygmomanometer. There was at least a 30-second interval between these two separate measurements, and thereafter the mean of the two measurements was considered the participant's blood pressure. At baseline and at each phase of the study, a blood sample was taken after a 12-14 hour overnight fast. Blood samples were taken in a sitting position according to the standard protocol and centrifuged within 30-45 min of collection. All blood analyses were done at the TLGS research laboratory on the day of blood collection. For the oral glucose tolerance test (OGTT), 82.5 g of glucose monohydrate solution (equivalent to 75 g anhydrous glucose) was administered orally to all subjects in each phase (excluding those with current use of a hypoglycemic agent) and plasma glucose was measured 2 hours later. The analysis of samples was performed using the Selectra 2 auto-analyzer (Vital Scientific, Spankeren, Netherlands). Fasting plasma glucose (FPG) and 2-hour post-load glucose (2hPG) were measured on the day of blood collection by the enzymatic colorimetric method using glucose oxidize. For lipid measurements, total cholesterol (TC) and triglyceride (TG) kits (Pars Azmoon Inc., Iran) were used. TC and TG were assayed using enzymatic colorimetric tests with cholesterol esterase and cholesterol oxidase, and glycerol phosphate oxidase, respectively. HDL-cholesterol (HDL-C) was measured after precipitation of the apolipoprotein B containing lipoproteins with phosphotungistic acid. All samples were analyzed when internal quality control met the acceptable criteria. Inter-and intra-assay coefficients of variation were 0.5% and 2 for TC and HDL-C and 0.6% and 1.6 for TG, respectively.

Definition of variables and outcomes

Based on the fasting and 2-hour plasma glucose (2hPG) results, subjects were categorized according to American Diabetes Association (ADA) criteria as having impaired fasting glucose (IFG) (100 mg/dL ≤FPG <126 mg/dL), impaired glucose tolerance (IGT) (140 mg/dL ≤2hPG <200 mg/dL), or diabetes (current use of hypoglycemic agent or FPG ≥126 mg/dL and/or 2hPG ≥200 mg/dL. Abnormal glucose tolerance was defined as having IFG or IGT.[16] Hypertension was defined as a systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg, or current use of an antihypertensive medication based on JNC7 (Joint National Committee 7).[17] BMI was categorized according to WHO recommendations as overweight (BMI=25-<30) and obese subjects (BMI$\geq$30).[18]

Statistical Analysis

Baseline variables were presented by follow-up diabetes status. Data with normally distributed parameters are presented as means and standard deviations, whereas values for trigylcerides (TG) were log-transformed because of a skewed distribution and expressed as a geometric mean. The mean value and proportions of the baseline variables were compared between subjects who developed diabetes and those who did not using the *t* test and chi-square test, respectively. To identify predictive factors for FPG over the period of follow-up, multiple linear regression analysis was carried out. A logistic regression analysis using a stepwise conditional method was used to calculate the odds ratio (OR) and 95% confidence intervals (CI) for incident diabetes associated with quartiles of anthropometric variables in 2 models: Model 1 was a multivariate model adjusted for age, family history of diabetes, hypertension, HDL-C and TG. Model 2 was a full model, adjusted for the previous variables plus abnormal glucose tolerance at the time of enrollment, considering that the latter is an important risk factor for diabetes. In each model, the subjects were categorized according to their WC, WHR, WHtR, and BMI quartiles. The first quartile was considered as a reference category with DM as outcome variable. Receiver operator characteristic (ROC) curves were used to compare the predictive power of each anthropometric variable after adjustment for age. All the statistical analyses except area under ROC comparisons were performed by SPSS 11.5 software package. The STATA software package version 8 was used to calculate the ROC curve of each anthropometric variable and 95% confidence intervals. *P* values (2-sided) less than .05 were considered statistically significant.

Table 1. Baseline characteristics by follow-up diabetes status.

Variable	Diabetic (n=114)	Nondiabetic (n=2687)	*P*
Age (years)	47.5 (11.98)	41.1 (12.7)	<.001
Body mass index (kg/m^2)	30.3 (4.3)	27.4 (5.1)	<.001
Waist circumference (cm)	95.9 (9.7)	87.2 (12)	<.001
Waist-hip ratio	0.89 (0.06)	0.83 (0.08)	<.001
Waist-height ratio	0.61 (0.06)	0.55 (0.08)	<.001
HDL-C (mg/dL)	40.9 (9.0)	45.4 (11.2)	<.001
Triglycerides (mg/dL)	181 (1.67)	129 (1.70)	<.001
Family history of diabetes (n, %)	49 (43)	722 (26.9)	<.001
Hypertension (n, %)	47 (41.1)	508 (18.9)	<.001
Smoking (n, %)	7 (6.1)	109 (4.0)	.2
Impaired glucose tolerance (n, %)	74 (64.9)	352 (13.1)	<.001
Impaired fasting glucose (n, %)	66 (57.9)	321 (11.9)	<.001

Data are mean (SD) (geometric mean for triglycerides) or number (percent). HDL-C: HDL-cholesterol; family history of diabetes: having a parent or sibling with diabetes; hypertension: blood pressure ≥140/90 mm Hg or usage of anti-hypertensive agents; smoking: being either current or ex-smoker.

RESULTS

The mean (SD) age of the women was 45.2 (12.9) years. Incident diabetes was diagnosed in 114 of participants (4.1%, 114/2801) at a median follow up 3.5 years (11 months to 6.3 years). We diagnosed diabetes in 15 subjects by FPG, in 53 subjects by 2hPG, in 19 subjects by both FPG and 2hPG, and in 27 subjects by noting use of hypoglycemic agents. In comparison to the subjects who did not attend the follow-up visit, those who attended had higher baseline values for age (42.6 vs. 40.2 years), BMI (27.6 vs. 26.8 kg/m^2), WC (88.4 vs. 86.5 cm), WHR (0.84 vs. 0.83), and WHtR (0.56 vs. 0.55) ($P<.05$ for all comparisons). However, the prevalence of hypertension and a family history of diabetes and the mean level of TG and HDL-C were not different between participants and non-participants.

The baseline characteristics of the study subjects according to their follow-up diabetes status are shown in Table 1 . Subjects who had developed diabetes at follow up had a significantly higher age, BMI, WC, WHR, WHtR, and a higher level of TG as well as lower HDL-C concentrations than nondiabetics. Diabetic women also had a higher prevalence of hypertension and a positive family history of diabetes, IGT and IFG. Smoking status was not significantly different in those who developed diabetes compared with those who did not develop diabetes. Each anthropometric index explained only about 11% of the variance in FPG after follow-up in a multiple regression analysis (Table 2). When baseline FPG was added to this analysis, this variance increased by about 17% (R^2=28%) (data not shown). In Table 3 the estimated OR and 95% CI for incident diabetes by quartiles of the anthropometric variables are presented for the two logistic regression models before and after adjustment for abnormal glucose tolerance. In the logistic regression analysis, the ORs (and 95% CIs) in model 1 were 4.8 (2.1-10.9), 6.7 (2.6-17.1), 8.7 (3.0-24.7), and 8.0 (3.1-20.6) for the fourth quartile versus the first quartile for BMI, WC, WHR and WHtR, respectively. Also, the OR of incident diabetes increased across all quartile of anthropometric indices (*P* for trend <.001). After further adjustment for abnormal glucose tolerance (model 2) the OR (95% CI) of the highest quartile of BMI, WC, WHR and WHtR, decreased to 3.1(1.3-7.2), 3.1(1.1-8.3), 4.0, 3.3 respectively, compared to values in model 1, but remained significant. However, the OR for incident diabetes increased across all quartiles of anthropometric indices in the second model (*P* for trend <.05), except for WHR which remained marginally significant (*P* for trend=0.05).

The baseline obesity indicators in this study were highly correlated with each other. BMI showed high correlation with WC (r=0.83), WHtR (r=0.83) and modest correlation with WHR (r=0.40). WHtR showed high correlation with both WC (r=0.96) and WHR (r=0.79) and finally WHR showed high correlation with WC (r=0.77) (data not shown). Therefore, because of the problem of co-linearity it was not possible to include them in the same regression model and ROC curve analysis was used to compare the predictive power of the different anthropometric variables. Figure 1 showed that only WHtR had a higher area under the ROC curve than BMI after adjustment for age (0.72 vs. 0.69). WC and WHR were considered equal to BMI in their power to predict type 2 diabetes. When the analysis was restricted to overweight and obese subjects, none of the central obesity indicators was confirmed to be superior to BMI.

DISCUSSION

This prospective study in Iranian women showed that BMI, WC, WHR and WHtR can predict incident diabetes. Our model identified those with a 3- to 4-fold increase in likelihood of developing diabetes during a median follow up of 3.5 years (11 months to 6.3 years); however, the overall predictive discrimination, (as the area under the ROC curves showed), for diabetes was better for WHtR than BMI.

Excess body fat is a main cause of metabolic disturbances such as type 2 DM.[5] As a simple and non-invasive method, anthropometric measurements have been used to assess general obesity (BMI) and central obesity (WC, WHR, WHtR).[19] BMI is reported as an indicator for identifying adults at risk of diabetes in many studies.[13,20] However, it has limitations because it does not distinguish overweight due to excess fat mass from lean mass.[21] In addition, some studies have shown that a high proportion of abdominal fat, particularly visceral fat, is a major risk factor for type 2 DM.[22] Therefore, other anthropometric parameters are used to assess excess visceral fat. WC and WHR are frequently used to estimate abdominal adipose tis-

Table 2. Multiple linear regression analyses between anthropometric and other independent variables with fasting plasma glucose as dependent variable.

	Body mass index			Waist circumference			Waist-hip ratio			Waist-height ratio		
	B	SE	*P*	B	SE	*P*	B	SE	*P*	B	SE	*P*
Anthropometric variables	0.35	0.05	<.001	0.17	0.02	<.001	15.71	3.50	<.001	23.44	3.53	<.001
Age (years)	0.17	0.02	<.001	0.14	0.02	<.001	0.160	0.02	<.001	0.14	0.23	<.001
Family history of diabetes	1.90	0.52	<.001	1.80	0.52	.001	1.94	0.53	<.001	1.80	0.53	.001
Hypertension	1.06	0.66	0.1	1.08	0.66	0.1	1.39	0.66	.03	1.09	0.66	.1
Triglycerides	0.01	0.003	<.001	0.01	0.003	<.001	0.01	0.003	<.001	0.01	0.003	<.001
HDL-C	-0.07	0.02	.001	-0.07	0.02	.002	-0.08	0.02	.001	-0.07	0.02	.001
	R^2=0.113			R^2=0.113			R^2=0.102			R^2=0.110		

*Median follow-up 3.5 years (11 months-6.3 years): Anthropometric variables (body mass index, waist circumference, waist-to-hip ratio, waist-to-height ratio) each included separately in four different models.

Table 3. Odds ratios (95% confidence intervals) for incident diabetes according to quartiles of anthropometric variables before and after abnormal glucose tolerance adjustment.

Variables	Quartiles	Diabetes (%)	Model 1[a] OR (95% CI)	*P* for trend	Model 2[b] OR (95% CI)	*P* for trend
Body mass index (kg/m²)	16.2-24.4	1.0	1.0	.001	1.0	.01
	24.5-27.4	3.5	2.6 (1.1-6.1)		1.8 (0.7-4.5)	
	27.5-30.5	3.6	2.2 (0.9-5.3)		1.6 (0.6-4.0)	
	30.6-48	8.2	4.8 (2.1-10.9)		3.1 (1.3-7.2)	
Waist circumference (cm)	58-79.9	0.7	1.0	.001	1.0	.04
	80-86.9	2.7	3.2 (1.2-8.9)		2.2 (0.7-6.3)	
	87-95.9	5.5	5.7 (2.2-14.8)		3.7 (1.4-9.9)	
	96-130	7.3	6.7 (2.6-17.1)		3.1 (1.1-8.3)	
Waist-hip ratio	0.57-0.78	0.6	1.0	.001	1.0	.05
	0.79-0.83	2.8	4.0 (1.3-12.1)		2.6 (0.8-8.1)	
	0.84-0.89	5.6	6.9 (2.4-19.7)		3.6 (1.2-10.7)	
	0.90-1.11	7.5	8.7 (3.0-24.7)		4.0 (1.3-11.8)	
Waist-height ratio	0.36-0.50	0.7	1.0	.001	1.0	.01
	0.51-0.55	2.1	2.4 (0.8-6.7)		1.4 (0.5-4.2)	
	0.56-0.61	5.2	5.1 (1.9-13.4)		2.7 (1.0-7.4)	
	0.62-0.84	8.7	8.0 (3.1-20.6)		3.3 (1.2-8.8)	

[a]Model 1: multivariate logistic regression model adjusted for age, hypertension, family history of diabetes, HDL-C and TG; [b]Model 2: full model adjusted for variables in model 1 plus abnormal glucose tolerance.

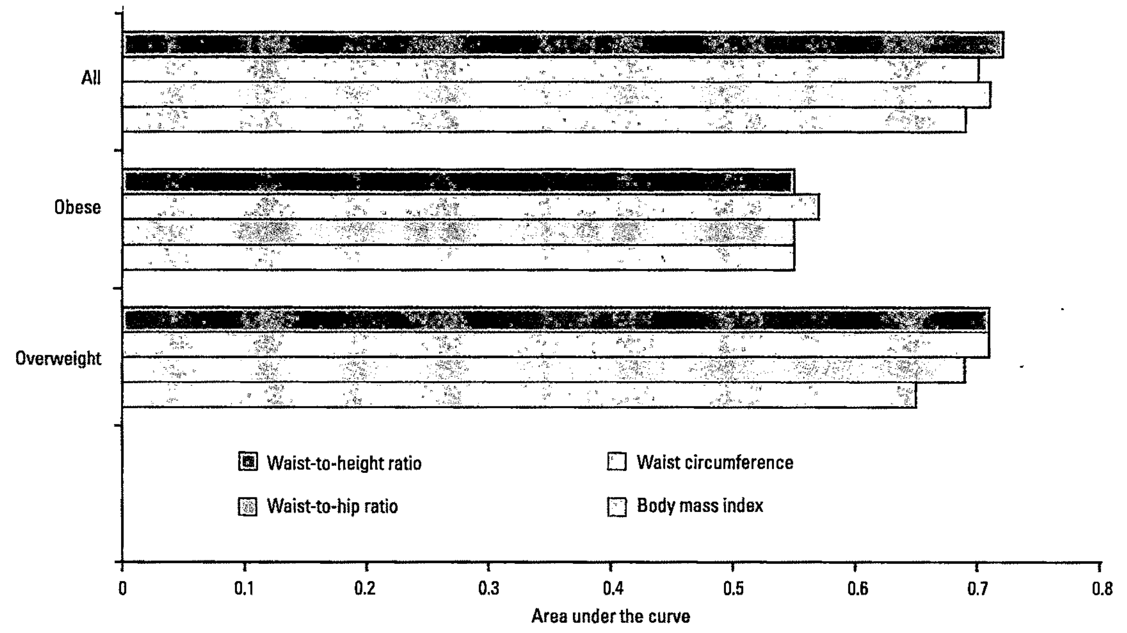

Figure 1. Area under the ROC curve for anthropometric variables in predicting diabetes after age-adjustment. BMI: body mass index, WC: waist circumference, WHR: waist–to-hip ratio, WHtR: waist-to-height ratio, Overweight: BMI=25-29.9 kg/m², Obese: BMI≥30 kg/m². * *P*<.05 compared to BMI.

sue. Recently, the Obesity in Asia Collaboration study showed that in white females measures of central obesity (WC, WHR) were more strongly associated with diabetes than BMI.[23] Also, WC was reported by Ford et al as a better predictor than BMI for prediction of metabolic syndrome, diabetes, cardiovascular disease and all-cause mortality.[24] However, other reports have shown conflicting results.[7,25] Lakka et al in prospective study, suggested WHR is a better index to predict coronary heart disease than WC and BMI.[26] Our full model (Table 3) showed that the OR for incident diabetes for the highest quartile versus the lowest quartile was greater for WHR followed by WHtR, WC and BMI, although the confidence intervals are wide and overlapping. In addition, despite a lower correlation with BMI and WC ($r=0.40$ and $r=0.77$, respectively), the WHR showed the same ability to predict diabetes as both BMI and WC, as discovered by Vazquez et al in a meta analysis.[9] However, our data confirmed that none of these anthropometric parameters are good measures for predicting future FPG (even when we considered baseline FPG). Considering the limitations of the OR (or relative risks or hazard ratio) as a method of assessing the importance of risk factors and for a more comprehensive picture of the clinical and public health relevance of anthropometric variables, we used ROC curve analyses to compare the predictive validity of these variables.[27] Among the central obesity variables only WHtR had a significantly larger area under the ROC curve than BMI. In line with our findings, Lin et al showed that in a Taiwanian population WHtR may be a better indicator for predicting cardiovascular risk factors than WC, WHR and BMI, especially for women.[28] Also, Lorenzo et al showed that area under the ROC curve for WHtR was better than WC for identifying diabetic women.[29] In a cross-sectional analysis, Schneider et al showed that WHtR may predict prevalent cardiovascular risk better than BMI, WC, and WHR.[30]

Furthermore, our study highlights that in overweight and obese subjects no central obesity variable is superior to BMI. Other studies suggest a stronger effect of body fat distribution on metabolic abnormality risk in normal-weight individuals compared with overweight or obese subjects.[31,32] Our data indicate that the WHtR appears to be a better predictor of DM risk than BMI in the population of women as a whole. The WHtR is simple to assess and is easier to calculate (no squared term is used in the formula) and WC requires only the removal of clothing around the waist. In addition, waist measurement is more sensitive to diet and exercise than BMI because any increase in muscle mass might cause a slight change in BMI, but result in definite changes in WC and thus in WHtR.

This study had some limitations. First, about 40% of the participants in our baseline cohort were excluded from analysis due to loss at followup. This group was healthier in their baseline characteristics; therefore, we may have overestimated the incidence of diabetes in our population. Second, the duration of follow-up was relatively short. Using a longer term follow up would provide stronger evidence although a similarly short follow up was seen in other studies.[33,34] Finally, since chronic diseases are heterogeneous and multifactorial, factors other than anthropometric variables, such as hereditary factors and menopausal state and lifestyle-related factors, should be considered.[35] This was the first population-based prospective study in Middle Eastern white women, which enhances the validity of our findings. In conclusion, abdominal obesity as measured by WHtR may be better predictors of type 2 diabetes compared to BMI in Iranian women. These simple, inexpensive and noninvasive measures of abdominal obesity is proposed to be incorporated in type 2 DM risk assessment.

Acknowledgments

This study supported by grant No. 121 from the National Research Council of Islamic Republic of Iran and by combined support of the National Research Council of Islamic Republic of Iran and Endocrine Research Center of Shahid Beheshti University of Medical Sciences.

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mini-review

Electrical cardioversion

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Ann Saudi Med 2009; 29(3): 201-206

External electrical cardioversion was first performed in the 1950s. Urgent or elective cardioversions have specific advantages, such as termination of atrial and ventricular tachycardia and recovery of sinus rhythm. Electrical cardioversion is life-saving when applied in urgent circumstances. The succcess rate is increased by accurate tachycardia diagnosis, careful patient selection, adequate electrode (paddles) application, determination of the optimal energy and anesthesia levels, prevention of embolic events and arrythmia recurrence and airway conservation while minimizing possible complications. Potential complications include ventricular fibrillation due to general anesthesia or lack of synchronization between the direct current (DC) shock and the QRS complex, thromboembolus due to insufficient anticoagulant therapy, non-sustained VT, atrial arrhythmia, heart block, bradycardia, transient left bundle branch block, myocardial necrosis, myocardial dysfunction, transient hypotension, pulmonary edema and skin burn. Electrical cardioversion performed in patients with a pacemaker or an incompatible cardioverter defibrillator may lead to dysfunction, namely acute or chronic changes in the pacing or sensitivity threshold. Although this procedure appears fairly simple, serious consequences might occur if inappropriately performed.

External electrical cardioversion (EEC) was first performed in the 1950s.[1] This early experience demonstrated that electrical energy externally delivered to the thorax could stimulate the heart. In 1955, Zoll et al successfully terminated ventricular fibrillation in a patient with externally applied defibrillation shocks. Kouwenhoven and colleagues discovered that a battery-powered direct current operated device could be fully portable.[2] Electrical countershocks can be delivered with either alternating current (AC) or direct current (DC) energy. Alternating currents are sinusoidal energy waveforms that switch between positive and negative polarity. The energy pulse lasts for approximately 200 ms once discharged. Alternating current defibrillation can cause significant myocardial damage due to the greater energy flux and duration.[3] Urgent or elective DC cardioversions have specific advantages, such as termination of atrial and ventricular tachycardia and recovery of sinus rhythm.

Mechanism of external cardioversion and defibrillation

The current external electrical cardioversion technique relies on the application of a selected amount of energy, which is generally between 50-360 J, via two electrodes (paddles). The mechanism of defibrillation is not known exactly. Zipes et al have suggested that failure to maintain the reentrant tachycardia by the remaining myocardial tissue after depolarization of a critical mass is the main factor in the mechanism of electrical defibrillation.[4] Another research group has suggested that the shock waves of defibrillation prolong refractoriness in a sufficient mass of myocardial tissue and, consequently, terminate ventricular fibrillation (VF).[3] Whether the mechanisms suggested for the termination of VF are similar to those of atrial fibrillation (AF) remains unknown.

A lower limit of vulnerability also exists for the ventricular myocardium. This is the minimum voltage required by an electrical stimulus to induce fibrillation during the vulnerable period. It was also observed that the strengths of these shocks at "the upper limit of vulnerability" were approximately equivalent to the shocks at defibrillation threshold. The upper limit of vulnerability hypothesis for defibrillation states that to defibrillate, a shock not only must halt the activation fronts of fibrillation, but it also must not reinitiate fibrillation by the same mechanism that a shock of the same strength during the vulnerable period of sinus or paced rhythm initiates fibrillation.[5]

Indications

Atrial fibrilation and atrial flutter

Currently, electrical cardioversion is mostly performed to convert AF and atrial flutter into sinus rhythm. AF, encountered in intensive care units after cardiac surgery, is not suitable for electrical cardioversion since it is paroxysmal. In the treatment of recurrent AF attacks, prevention of trigger mechanisms, application of specific antiarrhythmic therapies and improvement of electrolyte imbalance and hypoxia avert inappropriate cardioversion applications by blocking such episodes. AF treatment, on the other hand, includes anticoagulant therapy to minimize the risk of embolus and stroke during elective cardioversion. If AF persists for longer than 48 hours, anticoagulant therapy for 3 weeks is recommended with the international normalized ratio (INR) maintained >2.0. In case atrial activity is not achieved, therapy should be extended for 4 weeks, even after restoring sinus rhythm by electrical effective cardioversion.[6] A shorter-lasting AF (<48 hours) can alternatively be treated by heparinization and monitored by transesophageal echocardiography (TEE) prior to the cardioversion.[7] Any thrombotic formations within the left atrial appendix can be detected by TEE. The risk/benefit ratio should be assessed in all patients prior to cardioversion. Not observing a thrombus in TEE does not exclude the risk of embolus.

Venctricular and supraventricular tachycardia

Emergency electrical cardioversion is performed in unstable ventricular tachycardia that causes hemodynamic deterioration. If a patient with ventricular tachycardia is hemodynamically stable, sinus rhythm should be achieved by intravenous antiarrhythmics. Anticoagulation therapy is usually not necessary for cardioversion of ventricular tachycardia. Emergency electrical cardioversion is performed in unstable ventricular tachycardia that causes hemodynamic deterioration. The aim of ventricular tachycardia treatment is the prompt termination of this impairment. Electrical cardioversion should be the next step in case of unsuccessful antiarrhythmic treatment and vagotonic manoeuvres such as carotid sinus massage for sustained supraventricular tachycardia. The success rate with cardioversion of ventricular tachycardia is generally around 95%.[8]

Other rhythm disorders

Electrical shock treatment is ineffective in the termination of automaticity related tachycardies. Multifocal atrial tachycardias of this kind are generally confused with AF, which may lead to the inappropriate application of direct current (DC) shocks. Since electrical cardioversion may cause resistant VF in patients with digitalis toxicity, it is contraindicated in the presence of this condition.[8] Atrial flutter and ventricular tachycardia are tachycardias maintained by reentry circuits that may be terminated by local depolarization in the path of their circulating wavefronts.[8]

Factors affecting EEC success

Energy is a combination of voltage and current. The overall success of the electrical cardioversion is related to the size of electrodes (paddles), application site, transthoracic impedance, and the applied current. For a given amount of energy, the amount of current reaching the myocardium depends in part on the electrical impedance between the two defibrillator paddles. The distance between electrodes, electrode-skin interface and pressure (air is a poor conductor of electrical current), previous shocks (reduced impedance), time span between shocks (3-minute wait may cause resistance reduction), and physical characteristics (tall stature or increased BMI) decrease the rate of success.[9] The long-term success for AF is associated with the arrhythmia duration (>1 year) and the diameter of the enlarged left atrium (>5 cm).[8] Recurrence is more frequent in patients with untreated hyperthyroidism, mitral stenosis or congestive heart failure. Successful cardioversion is dependent on certain factors, of which time might be the most important one.[10] Since myocardial adenosine increases the defibrillation threshold, which is dependent on VF duration, its enhanced release may have a deleterious effect on defibrillation.[11] Another suggestion is that local changes in potassium concentration may increase defibrillation threshold.[12] If fibrillation time is prolonged in patients with AF, both postrepolarization and conduction delay occur due to global ischemia.[13] Energy is a combination of voltage and current.

Electrodes position

Defibrillator paddles can be used in different configurations, which affect the success rate of defibrillation. According to the International Liaison Committee on Resuscitation (ILCOR) guidelines, the sternal paddle should be placed just to the right of the upper sternal border below the clavicle and the apical paddle to the left of the nipple with the centre of the electrode in the midaxillary line.[14] Anteroposterior (parasternal and left infrascapular) positioning should be preferred for unsuccessful applications. It holds lower transthoracic impedance. By placing the paddles onto the chest wall, more current is delivered to the atria.

Thoracic impedance

Thoracic impedance is another important factor in treatment by electrical cardioversion. The paddle area is the main determinant of transthoracic impedance. Current is inversely related to impedance. The optimal paddle size varies between 8 cm to12 cm. Air between the chest wall and the paddles prevents the effective conduction of the shock wave by increasing transthoracic impedance. Any conductive material between paddles, such as gel or similar materials, increases conductance and decreases transthoracic impedance between the chest wall and the metal electrodes. Either special adhesive pads or special gels are used for this purpose. Contact between paddle area and chest wall must be provided. Gel between paddles should not touch in order to prevent current disorientation.[15] Such simple precautions cause a decrease in transthoracic impedance and increase the success of shock therapy. The resistance between electrode and the skin enhances the efficacy of electrical cardioversion therapy by providing appropriate pressure on impedance paddles. Transthoracic impedance decreases if the pressure applied on the defibrillator paddles is increased, if appropriate contact between paddles and chest wall is provided, and expiration period is less resistant compared to the inspiration. The shock wave is transmitted during the expirium period.[16]

Electrode size

In pediatric patients ≤10 kg, pediatric paddles should be used for electrical cardioversion, with an applied pressure of 2.9 kgf. If the child is >10 kg, adult-type paddles should be used, with an applied pressure of 5.1 kgf.[17] There are reports suggesting that chest shaving adds to the success of electrical cardioversion.[13] Sado et al stated that chest hair increased transthoracic impedance, which could be reduced up to 35% by shaving. It is recommended to shave the chest hair of such patients prior to defibrillation.[18]

Medications and sedations

In a pilot study, Sutton et al demonstrated that atropine administration increased the success rate of direct current cardioversion for atrial fibrillation.[19] Electrical cardioversion together with antiarrhythmics (such as amiodarone) may help in the maintenance of sinus rhythm. It has been demonstrated that verapamil treatment prior to defibrillation may prevent recurrence of early AF by affecting atrial remodeling.[20] A recent study showed that short-term verapamil treatment associated with propafenone or amiodarone seems to be useless for the prevention of recurrent AF after low energy intracardiac cardioversion.[21] Quinidine and propafenone seem to be effective in preventing immediate reinitiation of AF. Ibutilide may prevent shock failure, although neither ibutilide nor dofetilide seems to be effective in preventing immediate reinitiation of AF.[22] For refractory ventricular fibrillation or pulseless ventricular tachycardia, intravenous amiodarone 300 mg can be given initially, followed by a second dose of 150 mg. As an alternative, intravenous lidocaine 1-1.5 mg may be given, followed by 0.50-0.75 mg doses as needed up to a maximum of 3 mg.[23]

Patients may feel pain even at low energy levels (1 J). Electrical cardioversion with high levels of energy should never be performed in conscious patients, since it may cause lifelong emotional disorders and psychological trauma.[24] Administration of benzodiazepines, either alone or together with opiates, is not recommended in patients who will undergo electrical cardioversion. Propofol, an intravenous agent, seems to be an ideal drug for anesthesia since it acts rapidly, causes less laryngospasm, and loses its effect as soon as the treatment is ceased.[25] For elective EEC, deep sedation or anesthesia is required in stable patients. Mild sedation is sufficient for less painful procedures.[26]

Energy selection

Biphasic shock and monophasic shock

Transthoracic monophasic defibrillators have been employed for the management of ventricular arrhythmias. European Resuscitation Council guidelines recommend a 200 J, 360 J sequence with subsequent shocks at 360 J if the arrhythmia is uncorrected.[14] Recent studies of ventricular fibrillation have confirmed the superiority of various biphasic waveforms over monophasic pulses of quivalent or similar duration. Biphasic waveforms offer equivalent or superior efficacy at lower energy and peak voltage than their monophasic counterparts.[27] Biphasic waveform shocks with a fixed energy of 150 J were as effective as conventional sequential monophasic waveform with progressive energy levels of 200, 300 and 360 J for successful defibrillation. However, the low-energy biphasic waveform shocks significantly decreased the severity of postresuscitation myocardial dysfunction.[28]

An initial energy level for AF of 100-200J is recommended. The success rate of electrical cardioversion is approximately 50%. In a recent study, an initial energy level of 360 J was suggested for persistent AF lasting more than 48 hours.[29] In a study comparing 50 J with 100 J for the conversion of atrial flutter to sinus rhythm, 100 J was considered the best initial energy level.[30] Energy set between 100-200 J is recommended for monomorphic ventricular tachycardia, although lower energy levels may be effective as well.[31] On the other hand, the initial defibrillation threshold is suggested to be 200 J in polymorphic ventricular tachycardia or VF. The energy level should be 1-2 J/kg in children with ventricular tachycardia without a pulse or VF.[14] Low energy levels produce lesser myocardial damage and post-resuscitation myocardial dysfunction.[28] Synchronization with R wave is mandatory to prevent resistant VF that could be induced by shock wave and T wave overlapping, called a vulnerable period, if a QRS complex appeared during electrical cardioversion. Careful electrocardiographic (ECG) evaluation is required to avoid inappropriate shock therapies in patients with sinus or automatic tachycardia. Shock therapy should not be performed if only one derivation is being monitored in hemodynamically stable patients. Recurrent inappropriate and ineffective shock therapies can have dangerous consequences. Pharmacological prevention of atrial flutter recurrences is quite difficult. The typical recurrent atrial flutter should be treated by catheter ablation. The presence of a structural cardiac anomaly together with continuous ventricular tachycardia or VF holds a risk for sudden death. An implantable cardioverter defibrillator (ICD) should be considered if there is no identifiable cause. Internal cardiac cardioversion is safe and effective in patients with resistant AF.[32] A study comparing the efficacy of external and internal cardioversion in AF showed that internal cardioversion was more effective in restoring sinus rhythm.[33] Loss of QRS voltage after EEC or defibrillation was suggested to be of electrical origin or consequent to an edematous area on the chest wall due to trauma. Another proposed reason is myocardial stunning.[34]

Management of patients with failed EEC or resistant patients

The risks and benefits of recurrent electrical shock therapy must be taken into account. Unnecessary recurrent DC shock treatment should be avoided. The upper shock limit applied by several defibrillators currently used is 360 J, and the waveform is monophasic. As technology progresses, biphasic shock waves are employed. ICDs are the best example of such application. The transvenous activity, the accessible implantation, and the smaller dimensions have contributed to the wide therapeutic adoption of ICD devices. Lown mentioned that higher energy levels were required to terminate AF in congestive heart failure. Restoration of cardiac compensation and achievement of a dry weight before cardioversion increased the success rate. In cases of polycytemia, it may be difficult or impossible to revert until adequate phlebotomy lowers the hematocrit to less than 50. Patients with severe mitral valve disease having giant scarred atria who have had valve repair or replacement are recalcitrant to cardioversion and do not persist in sinus rhythm.[31] The rate of sinus rhythm re-establishment via internal cardioversion in AF, which is resistant to 360 J, varies between 70% and 80%.[35] The use of biphasic waves through multipolar catheters, which are placed within the right atrium and coronary sinus, enhances the success rate of cardioversion by markedly reducing the required energy. Despite these low energy levels (2-3 J), sedation and anesthesia are necessary because of the painful procedure.

In new devices, the electrodes are placed within the right atrium and the left pulmonary artery for internal cardioversion. Superior homogeneous electrical dispersion and cardioversion effectiveness have been reported with such electrode placement.[9] In a multicenter study by Bardy et al, it was reported that automatic external defibrillators, which use biphasic wave shocks, required lower energy than those devices using monophasic waves.[36] A biphasic shock waveform is known to reduce the ventricular defibrilation testing.[37] Since synchronization with the R wave is not feasible for these devices, they are not applied in regular tachycardia with R waves.

Complications and contradictions of cardioversion

Complications are minimal. Potential complications include VF due to general anesthesia or lack of synchronization between the DC shock and the QRS complex, thromboembolus due to insufficient anticoagulant therapy, non-sustained VT, atrial arrhythmia, heart block, bradycardia, transient left bundle branch block, myocardial necrosis, myocardial dysfunction, transient hypotension, pulmonary edema and skin burn. Pain at the application site is associated with the number of applications.[38] EEC is contraindicated in case of the presence of left atrial thrombus and insufficient anesthesia in stable patients.

Special conditions

Arrhythmias in intensive care patients

Atrial and ventricular tachycardias are frequent in patients being treated at intensive care units due to the presence of multiple triggers. Hypoxia, endogenous or exogenous catecholamines, congestive heart failure, fever and pulmonary embolus are particular causes of tachycardia. Patients unable to receive the drugs orally or with poor absorption are more prone to side effects, such as hypotension, which may especially occur with intravenous drugs like amiodarone. Rapid and throughout examination prior to the electrical cardioversion is important. Improvement of trigger and underlying etiologic factors enhances the success rate of cardioversion.[8] It should be kept in mind that many consecutive shocks and anesthesia in recurrent doses may worsen hemodynamic status in those patients.

Internal cardiac cardioversion is safe and effective in patients with resistant AF.[34] A study comparing the efficacy of external and internal cardioversion in AF showed that internal cardioversion was more effective in restoring sinus rhythm.[35]

Cardioversion in Pregnancy

Some investigators have reported that electrical cardioversion is safe during pregnancy.[39] Cardioversion between 50 J and 300 J applied at various pregnancy phases revealed negligible effects on the fetus, which means harmful electrical current may not reach the fetus.[40,41] Almost 100 years ago, in his animal experiments, Garrey emphasized that a critical myocardial mass would be required for VF. For this reason, it can be assumed that cardioversion may not affect the fetus.[42]

EEC in patients with pacemakers

Electrical cardioversion performed in patients with a pacemaker or ICD may lead to dysfunction, namely acute or chronic changes in the pacing or sensitivity threshold.[43] If a patient with a pacemaker should undergo cardioversion, the function and leads of the device should be checked, along with high voltage programming. Pacemaker mode should be switched to VOO or AOO if suitable. During cardioversion, the defibrillator paddles should be placed at a minimum of 15 cm apart from the pacemaker. They should be positioned perpendicularly to the anterolateral, anteroposterior or endocardial leads. A 5-minute interval between two shock wave applications is required. The pacemaker battery and lead functions must also be checked after cardioversion. A high threshold should be maintained for at least 4-6 weeks. In case of pacemaker and lead dysfunction, lead replacement is the advised procedure.[43] During cardioversion, patients with a pacemaker or ICD may be exposed to burns in the myocardial tissue where the pacemaker lead is attached if electrical current is delivered through it.

Conclusions

Cardioversion/defibrillation equipment is of the utmost importance to clinicians. Electrical cardioversion is a life-saving when applied in emergency circumstances. In elective cardioversion, accurate tachycardia diagnosis, careful patient selection, adequate electrode (paddles) application, determination of the optimal energy and anesthesia levels, prevention of embolic events and arrythmia recurrence, and airway conservation increase the success rate while minimizing possible complications. Although this procedure appears fairly simple, serious consequences might occur if inappropriately performed.

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brief report

Black ant stings caused by *Pachycondyla sennaarensis*: a significant health hazard

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Ann Saudi Med 2009; 29(3): 207-211

Several species of ants cause stings, but not all lead to allergic reactions. We present a series of cases of allergic reactions following insect bites or stings that presented to our emergency department and that were caused by the black samsum ant (*Pachycondyla sennaarensis*). Reactions ranged from mild allergic reactions to severe anaphylactic shock. Patients were treated with subcutaneous epinephrine 0.3 mg, intravenous methylprednisolone 125 mg, intravenous diphenhydramine HCl 50 mg, and intravenous normal saline as appropriate. These cases illustrate the range of clinical presentations to black ant stings, which can include severe reactions, indicating that ant stings are a significant public health hazard in Saudi Arabia. Physicians in the Middle East and Asia need to be aware of ant stings as a cause of severe allergic reactions.

Allergic reactions, ranging from mild allergic reaction mild hives to severe anaphylaxis and shock, are common presenting problems to emergency departments a well known medical problem facing physicians. Causes have been attributed to drugs, food, contrast agents, exercise and stress, and stings from bees, wasps and ants.[1] Several species of ants are capable of stinging, but not all lead to allergic reactions. Fire ants have been studied thoroughly and are considered responsible for most of allergic reactions secondary to ants in the United States.[2] Systemic reactions with fire ant stings occur in about 4 of 100 000 exposed individuals, and more than 80 fatalities have been reported from fire ant-induced anaphylaxis.[2] In China and Korea another species of ant known as *Bachycondayla chinensis* is a major cause of allergic reactions. In addition, *Myrmecia pilosula* (jack jumper ant) in Australia is a known health hazard.[1-3]

We have noted a significant number of unidentified insect exposures in our emergency department that have led to different degrees of allergies. Therefore, we decided to identify the cause of these stings or bites by obtaining samples of the causal agent for identification. In this study we selected a case series of patients that were able to identify the cause of the sting as a black ant. The black ant specimens were selected carefully for photography and identification. The identification was done by a certified entomologist in the Department of Zoology, College of Science, King Saud University in Riyadh. All the specimens were collected from the eastern region of Riyadh in year 2006-2007. The species was then identified and its characteristics were described. The cases we report are cases that we encountered during our practice, ranging from mild to severe allergic reaction secondary to these black ant bites (Table 1). We note that the cases ranged from mild to severe allergic reaction requiring epinephrine. We also present a suggested treatment and follow-up algorithm.

CASE 1

A 34-year-old Saudi male presented to the emergency department complaining of generalized body rash and itching starting 30 minutes after being stung by a black ant at home. He had no other complaints such as shortness of breath, lightheadedness, chest pain or palpitations. He had no previous medical or surgical history and was not known to be allergic to any medication, food or any other allergen and never had an allergic reaction in the past. On examination he displayed normal vital signs and had a pruritic, urticarial rash over the four limbs and trunk. The patient was given methylprednisolone 125 mg and diphenhydramine HCl 50 mg intravenously and kept in the ER observation area for four hours until his symptoms started to subside and then he was discharged home with instructions on how to avoid future ant bites.

CASE 2

A 27-year-old Saudi female presented one hour after being stung by a black ant at her neighbor's home. She complained of an itchy rash and lightheadedness. These complaints started minutes after being stung. She had no medical history or allergic reactions in the past. Her initial vital signs were a blood pressure of 105/75 mm Hg, a heart rate of 99 per minute, a respiratory rate of 22 per minute, a temperature of 36.6°C and an oxygen saturation of 98% on room air. After 15 minutes of presentation the patient complained of dizziness and her blood pressure dropped to 77/44 mm Hg. The patient had a generalized urticarial rash mainly over the upper limbs and abdomen. The rest of her physical examination was unremarkable. She was managed by 0.3mg subcutaneous epinephrine and a bolus of 1 liter of normal saline after which her blood pressure returned to normal. She was given methylprednisolone 125 mg and diphenhydramine HCI 50 mg intravenously and was observed in the emergency department for four hours and then discharged home in stable condition.

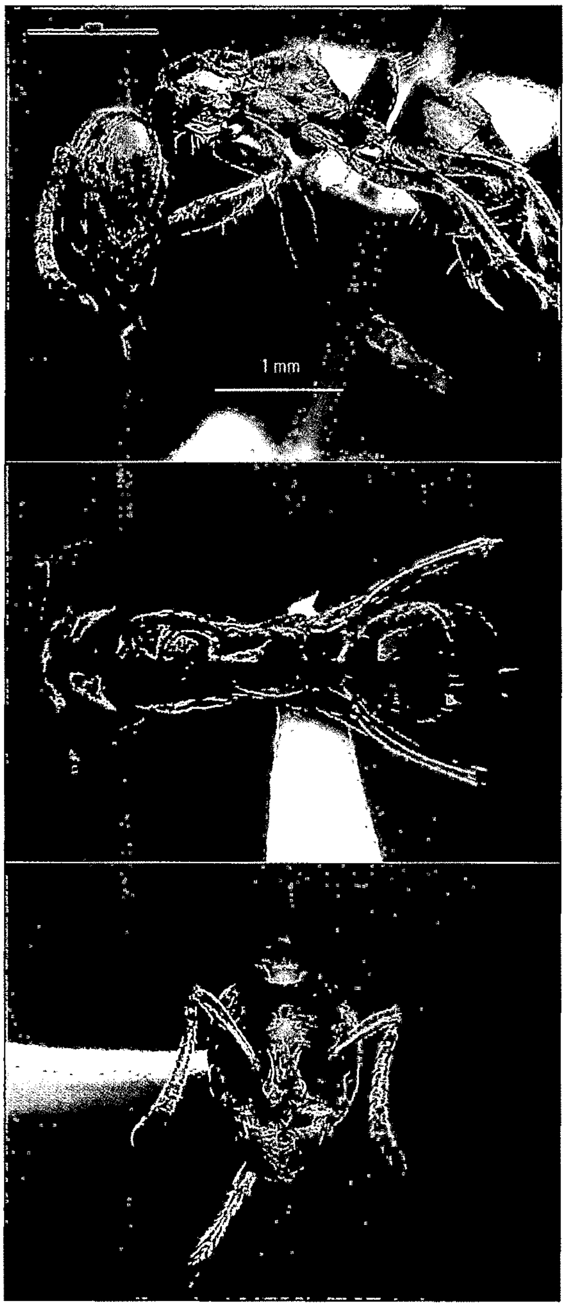

Figure 1. Photograph of *Pachycondyla sennaarensis* (black samsum ant). Used with permission of Mike J. Lush, sifolinia.blogspot.com, 2009.

CASE 3

A 27-year-old Saudi female presented to our emergency department with a chief complaint of breathlessness, dizziness and itching and redness over the body after an ant sting 2 hours prior to presentation. Symptoms started about 5 minutes after the sting. Her medical history included allergic rhinitis. Physical examination showed an anxious and restless woman with stable vital signs and generalized urticaria (Table 1). She was managed by intravenous fluid therapy, subcutaneous epinephrine injection, methylprednisolone 125 mg and diphenhydramine HCI 50 mg intravenously. After observing her for six hours, she was discharged in good condition.

CASE 4

A 49-year-old Saudi female presented to our department after a black ant sting, complaining of shortness of breath and generalized swelling, mainly of the face and lips along with an itchy rash that started 10 minutes after being stung by a black ant at her home. This was the sixth presentation for this patient to our department suffering from anaphylaxis secondary to a black ant stings. Her medical history included a cirrhotic liver secondary to hepatits C virus infection. Initial vital signs were normal with wheezing evident on chest auscultation (Table 1). However, the patient became more distressed and the swelling increased and her level of consciousness deteriorated rapidly, so the patient underwent endotracheal intubation. The team intubating her faced a difficult intubation. They only managed to insert a 6.5 mm endotracheal tube due to airway edema. She was started on epinephrine infusion, methylprednisolone 125 mg and diphenhydramine HCI 50 mg intravenously. She was admitted to the intensive care unit

Table 1. Clinical summary of cases presenting with allergy secondary to the sting of the *Pachycondyla sennaarensis*.

Case	1	2	3	4
Demographics	34 y/o male	27 y/o Saudi female	27 y/o Saudi female	49 y/o Saudi female with liver cirrhosis
Presentation	Itchy rash	Itchy rash, lightheadedness	Shortness of breath, lightheadedness, itchy rash	Shortness of breath, swelling of upper airway
Onset of symptoms after sting	30 minutes	Few minutes	Few minutes	10 minutes
Vital signs	BP: 120/80 mm Hg HR: 80/minute RR: 18/minute Temp: 37°C O_2 sat: 99% on RA	BP: 105/75 mm Hg HR: 99/minute RR: 22/minute Temp: 36.6°C O_2 sat: 98% on RA BP dropped to 77/44 after 30min	BP: 130/85 mm Hg HR: 105/minute RR: 24/minute Temp: 36°C O_2 sat: 98% on RA	BP: 95/65 mm Hg HR: 110/minute RR: 28/minute Temp: 37°C O_2 sat: 99% on RA
Physical examination	Airway: Patent Chest : Clear Skin: Urticarial rash spread over limbs and trunk	Airway: Patent Chest: Clear Skin: Urticarial rash spread over limbs and abdomen	Airway: Patent Chest: Clear Skin: Generalized urticaria	Airway: Angioedema Chest: Wheezy chest Skin: Clear Level of consciousness deteriorated.
History of allergies	No past history of allergy	No past history of allergy	Allergic rhinitis	Black ant (6th presentation with anaphylaxis)
Causative agent	Black ant brought by patient for identification	Black ant brought by friends for identification	Black ant brought by patient for identification	Black ant brought by family for identification
Management	Antihistamine, systemic steroids	Subcutaneous epinephrine injection, intravenous fluids, antihistamine, systemic steroids	Subcutaneous epinephrine injection, Intravenous fluids, antihistamine, systemic steroids	Endotrachial intubation, epinephrine infusion, antihistamine, systemic steroids
Disposition	4 hours observation	4 hours observation	6 hours observation	ICU admission
Discharge treatment	Antihistamine, instructions to avoid black ant exposure	Antihistamine, instructions to avoid black ant exposure, follow up primary health care	Antihistamine, instructions to avoid black ant exposure, follow up primary health care	Epipen kit, antihistamine and instructed to eradicate black ants around her house and surroundings, and not to walk barefoot, follow-up immunology clinic

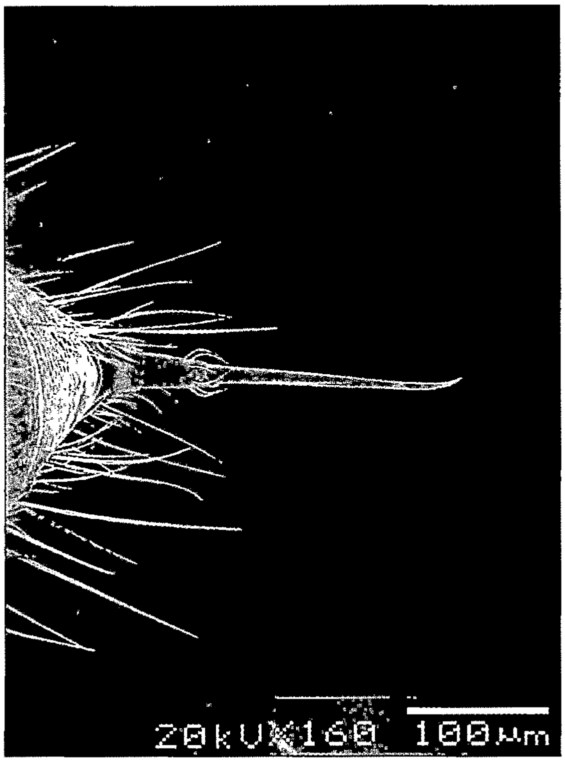

Figure 2. Electron microscope image of the stinger of *Pachycondyla sennaarensis* which injects allergenic venom. From the Museum of Entomology in Department of Zoology, College of Science, King Saud University, Riyadh, Saudi Arabia (Courtesy of Dr. M. Khalifa).

for two days, and after extubation she was observed on the floor for another two days. She was discharged with an EpiPen kit and strongly advised not to walk barefoot and to perform pest control and eradication in her house and its surroundings.

DISCUSSION

Pachycondyla sennaarensis belongs to the subfamily Ponerinae, a species that is widely distributed in tropical and subtropical regions worldwide. It is believed to be indigenous to Southeast Asia, but has been reported from all of the Arab Gulf countries including Kuwait, Qatar, the United Arab Emirates, Oman, Yemen and Saudi Arabia.[4] In Saudi Arabia it seems to prefer areas of human habitation. Although the ant is a scavenger in nature, it stings human beings as a defensive behavior.[5] Recently, several anaphylactic cases following black (samsum) ant stings were reported in local clinics in Saudi Arabia, some of them critical.[6] This ant has been observed around and inside houses and in hospital residence areas in many locations in the Al Riyadh region. The risk to humans from a particular species probably depends on complex interactions between the likelihood of human contact, insect aggression, efficiency of the venom delivery apparatus, and venom allergenicity.

The most important morphological features of this ant are the large eyes and mandibles with a dorsolateral

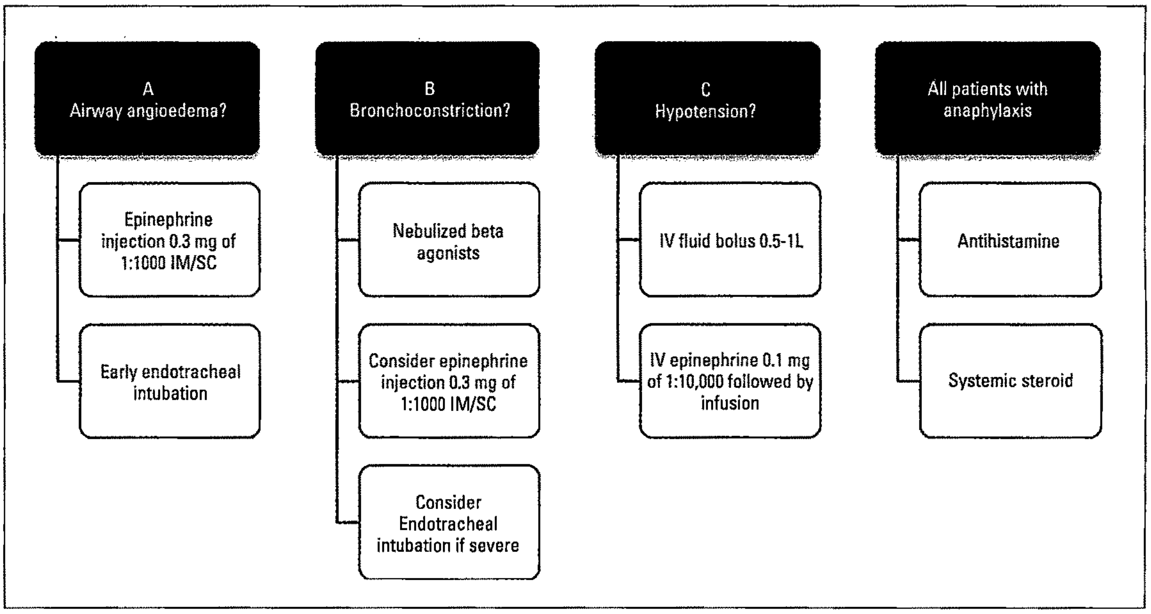
A
Airway angioedema?
Epinephrine injection 0.3 mg of 1:1000 IM/SC
Early endotracheal intubation
B
Bronchoconstriction?
Nebulized beta agonists
Consider epinephrine injection 0.3 mg of 1:1000 IM/SC
Consider Endotracheal intubation if severe
C
Hypotension?
IV fluid bolus 0.5-1L
IV epinephrine 0.1 mg of 1:10,000 followed by infusion
All patients with anaphylaxis
Antihistamine
Systemic steroid

Figure 3. Simple algorithm for treating patients presenting with acute anaphylaxis.

pit, and the presence of a deep mesopropodal furrow (Figure 1). It does not bite; instead, it injects venom through a stinger (Figure 2), like fire ants and other Hymenoptera. The mechanism of the reaction to the sting of the black ant *Pachycondyla sennaarensis* is a type I IgE-mediated hypersensitivity and the diagnosis can be confirmed by skin tests and specific IgE determination.[7,8]

The imported fire ant is a significant health problem in the southern United States.[2] The venom from fire ants contains several allergenic proteins, which can cause anaphylaxis in allergic individuals. The safety and effectiveness of several immunotherapy options have been documented for fire ant stings.[9,10] However, research has shown that patients who have had an anaphylactic reaction to a *Pachycondyla* species ant might not benefit from immunotherapy with an imported fire ant extract.[10] Immunotherapy with the extract of *Pachycondyla* species ants is expected to be highly effective. Ant venom immunotherapy is feasible and highly efficacious.[10] However, the limited geographical distribution of each species presents a major challenge to making venom extracts available for clinical use.[12]

In this study we confirmed the exact species, the venomous nature of its sting and the range of clinical manifestations associated with black ant stings. The acute emergency treatment depends on the manifestation that develop. The acute treatment is summarized in Figure 3. Patients need to be followed-up by AN immunologists for these cases to be managed appropriately and to document if they develop secondary reactions. The cases were referred to primary health care in this case series prior to documenting that the cause of the allergy was an ant bite.

The study of ant allergy in Asia and the Middle East is in its infancy. Clinicians in these countries need to be aware of ant stings as a cause of severe allergic reactions. Certain species that cause allergic reactions deserve further research. The allergens in the venom of the different ant species need to be identified. We should aim for improved understanding of the epidemiology of ant-sting anaphylaxis, formulation of better diagnostic tests and possibly the introduction of immunotherapeutic strategies. We believe these types of studies are required to find an effective treatment or prophylaxis against ant stings as it is a health hazard that can lead to severe morbidity and mortality. This study confirms that public health problems due to severe ant sting anaphylaxis in this region are due to the ant species *Pachycondyla sennaarensis* (samsum ant).

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Prevalence of allergic fungal sinusitis among patients with nasal polyps

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Ann Saudi 2009; 29(3): 212-214

BACKGROUND: Nasal polyposis is a common problem in the eastern province of Saudi Arabia. Since allergic fungal sinusitis (AFS) can present with unilateral or bilateral nasal polyps, it is important to be aware of the prevalence of AFS in patients with nasal polyps.
PATIENTS AND METHODS: The medical records of 91 patients with nasal polyps admitted for functional endoscopic sinus surgery were reviewed. The diagnosis of AFS was considered if histopathology showed the presence of eosinophillic mucin-containing hyphae. The following data were collected: presence of associated asthma, IgE levels, grading of CT scan findings, and operative details.
RESULTS: Histopathological diagnosis was positive for AFS in 11 of 91 patients 12.1%. There was a highly significant statistical difference in IgE levels between patients suffering AFS and chronic hyperplastic rhinosinusitis with nasal polyps ($P<.0001$). The overall incidence of recurrence of polypi was 50.5% (45 of 89 patients who had follow up for a minimum of one year) and the rate of recurrence in patients with AFS was 54.5% (6 of 11 patients with AFS). There was a significant direct relationship between the CT grading of nasal polyps and recurrence, with a recurrence rate of 60.7% (34 of 56) in patients with grade III nasal polyps.
CONCLUSION: This study showed that the prevalence of AFS among patients with nasal polyps is 12.1%, and suggests that CT grading of nasal polyps can be used as a prognostic factor for disease recurrence.

Allergic fungal sinusitis (AFS) is a type I hypersensitivity reaction to fungal antigens in which patients usually present with unilateral or bilateral nasal polyps.[1] It is important to be aware of the prevalence of AFS in patients with nasal polyps. Ferguson stated that the simplest and most straightforward requirement for defining patients as having AFS is the presence of eosinophilic mucin with hyphae.[2] Kuhn and Javer studied whether specific IgE to fungal species was superior to total IgE in predicting persistence or recurrence.[3] They found that total IgE was generally most sensitive. Asthma associated with AFS is estimated to range from 20% to 40%.[4] Bee-See et al found a prevalence of AFS in adult Malaysians with chronic rhinosinusitis of 26.7% and a prevalence of associated asthma of 25%.[5] In another study performed by Chen et al, AFS was several-fold higher in the southern compared with the northern United States.[6] As the prevalence of AFS among patients with nasal polyps has not been estimated in the Middle East and due to the potential for disease complication in cases of AFS, we decided it was important to find the prevalence of this disease among patients with nasal polyps.

PATIENTS AND METHODS

Between January 2004 and May 2007, 95 patients were admitted to King Fahd Hospital of the University with a diagnosis of unilateral or bilateral nasal polyps for functional endoscopic sinus surgery (FESS). The following data were collected; age, sex, CT scan findings, IgE level, operative details, final diagnosis based on histopathological findings of the removed tissue specimens and mucin (when present), recurrence in patients that were followed up for one year or more, presence of associated asthma, and the results of fungal cultures in suspected cases of AFS.

CT scan staging of nasal polyps was based on the staging of Lildholdt et al[7] in which nasal polyps are classified according to a fixed anatomical landmark, namely the middle and inferior turbinates (grade 1: small polyps extend just below the free edge of the middle turbinate; grade 2: medium size polyps reaching between the upper and lower edges of the inferior turbinate and grade 3: large polyps reaching below the lower edge of the inferior turbinate. AFS was considered if the histopathology confirmed the presence of eosinophilic mucin-containing hyphae.[8]

Data was analyzed using SPSS version 15. For descriptive statistics, the mean and standard deviation are shown. For comparisons, the t test for independent variables, analysis of variance and chi-square were used as appropriate. The level of significance was set at <.05.

RESULTS

The medical records of 91 patients were included in this retrospective study as the remaining 4 records were missing most of the data. The 91 patients ranged in age from 11 to 62 years with a mean (SD) age of 37.1 (13.2) years. There were 30 females (33.0%) and 61 males (67.0%). CT scan grading was available for all patients. Based on the final histopathology report, the incidence of AFS among patients with nasal polyps was 12.1% (11/91 patients). The remaining 80 patients showed histopathological features of chronic hyperplastic rhinosinusitis. An estimated IgE level was found in 77 records. The mean (SD) IgE level was 242.1 (381.3) IU/mL for patients with chronic rhinosinusitis (66 patients), and 820.2 (752.8) IU/mL for AFS patients (11 patients). An independent sample test showed a highly significant difference (*P*<.0001).

Eighty-nine patients were followed up for one year or more with mean of 16 months. The overall recurrence rate in these patients was 50.5% (45 patients). The recurrence rate in patients with AFS was 54.5% (6 of 11 patients), while the rate of recurrence in non-fungal nasal polyposis was 50% (39 of 78 patients) (Table 1).

Sixty-six patients (72.5%) were non-asthmatic and 25 patients (27.5%) were asthmatic. Only one patient with AFS had an associated asthma (9% of all patients with AFS). Statistically, it was found that asthma is not a significant factor in nasal polyposis or AFS (*P*>.05). In 8 of 11 cases of AFS *Aspergillus* species were demonstrated in fungal cultures. In the remaining 3 cases, cultures were negative.

DISCUSSION

Nasal polyps are a common problem with different etiologies. It is important to try to estimate the incidence of AFS among patients with nasal polyps. In this retrospective study we were able to collect data from the medical records of 91 patients admitted with the preoperative diagnosis of nasal polyps in the period from January 2004 to May 2007 for endoscopic sinus surgery. A histopathologically valid diagnosis was found in the 91 patients medical records and 11 patients (12.1%) were proven to have AFS. Bee-See et al (2005) found that the incidence of AFS in adult Malaysian patients with refractory rhinosinusitis was 26.7%, the presence of allergic mucin was the tool for diagnosing AFS, although they found fungus in secretions in only 5 patients (16.7%) and in nasal secretions and in surgical specimens in 11 (36.7%).[5] On the other hand, Braun et al (2003) found an incidence of AFS among patients with nasal polyposis of 7%.[9] This variability in incidence may be due to different techniques in diagnosis and differences in geographical distribution.

Our study showed that the total IgE was significantly higher in patients with AFS than those with chronic rhinosinusitis. These results are in agreement with Ferguson, who stated that total IgE in patients with AFS is frequently elevated with a mean of 668 IU/mL. with the normal being less than 125 IU/mL.[10] Moreover, Schbert found that total IgE correlated significantly with the severity of the disease, and that an increase of 10% or more in total serum IgE during the follow-up period was a strong predictor of recurrence and the need for surgical intervention.[11]

Although we think that total IgE is important in the diagnosis and prognosis of AFS, we recognize that the large standard deviation makes it difficult to use it as a diagnostic tool. This marked variability may in part be attributed to fluctuation in disease activity. However, total IgE might be helpful to differentiate between eosinophilic mucin rhinosinusitis and AFS, where there are elevated levels in cases of AFS.[1]

In this study, the overall recurrence rate for nasal polyps was 50.5% (45 out of 89 patients). Six of 11 patients (54.5%) with AFS showed recurrence within one year,

Table 1. CT scan grading and recurrence of polyps after 1 year or more of follow-up in 91 patients with nasal polyposis.

	CT scan grading, n (%)			Total
Patients	I	II	III	
All[a]	1 (1.098)	32 (35.2)	58 (63.7)	91
Recurrence[b]	0	11 of 32 (34.4)	34 of 56 (60.7)[c]	45*
Non-fungal polyposis[a]	1 (1.282)	26 (33.3)	51 (65.4)	78
Recurrence[b]	0	8 of 26 (30.8)	31 of 51 (60.8)	39
Allergic fungal sinusitis[a]	0	6 (54.5)	5 (45.5)	11
Recurrence[b]	0	3 of 6 (50%)	3 of 5 (60%)	6

[a]Percentage of totals in right column. [b]Percentage of total for grade category. [c]34/56; 2 patients lost to follow-up.
**P*<.05 across row

while the recurrence rate in patients with hyperplastic rhinosinusitis was 50% (39 of 78 patients). This was found to be insignificant statistically. In a retrospective study, Wynn and Har found a recurrence rate in patients with nasal polyps of 60% after 40 months of follow up.[12] The lower rate in our study may be due to the shorter period of follow-up. Although Ferguson reported that the recurrence of AFS following surgery alone is very high,[2] we found no accurate figure for the rate of recurrence for AFS in the literature. In applying the grading system for nasal polyps described by Lildholdt et al[7] we found that there was a significant increase in the rate of recurrence with the increase in grade, suggesting that grading system could be used for prediction of recurrence of nasal polyps.

Asthma was found to be associated with nasal polyps in 25 patients (27.5%) and only in one patient with AFS (9%), suggesting that asthma is not an important associated pathology in allergic fungal sinusitis. In most of the literature, the rate of associated asthma in cases of AFS ranges from 30% to 40%. The lower incidence of associated asthma in our study may be due to the study having few patients to provide an accurate incidence of associated asthma. If asthma is not an important associated pathology, the high incidence of associated asthma in the literature may be related to the mixing of AFS and non-fungal eosinophillic mucin rhinosinusitis in which the incidence of associated asthma is 93%.[10]

Aspergillus was the only species found in 8 of the 11 cases diagnosed as AFS. These results are in agreement with the results of Ferguson et al, who noted that there appears to be a geographical variability in the incidence of AFS and fungal species associated with the disease process. In the United States, dematiaceous fungi are the most common while Aspergillus species cause most cases reported in the Middle East.[13] In conclusion, this study showed that the prevalence of AFS among patients with nasal polyps is 12.1%, and IgE level was higher in patients with AFS than those with chronic hyperplastic rhinosinusitis. It suggests that CT grading of nasal polyps can be used as a prognostic factor for disease recurrence and asthma is not significantly associated with nasal polyps.

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brief report

Osteoporosis prophylaxis in patients receiving chronic glucocorticoid therapy

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Ann Saudi Med 2009; 29(3): 215-218

BACKGROUND AND OBJECTIVES: Glucocorticoid-induced osteoporosis (GIOP) is the most common form of secondary osteoporosis, yet few patients receive proper measures to prevent its development. We retrospectively searched prescription records to determine if patients receiving oral prednisolone were receiving prophylaxis or treatment for osteopenia and osteoporosis.

METHODS: Patients who were prescribed $\geq$7.5 milligrams of prednisolone for 6 months or longer during a 6-month period were identified through the prescription monitoring system. Demographic and clinical data were extracted from the patient records, and dual energy x-ray absorptiometry (DEXA) scans were retrieved, when available. Use of oral calcium, vitamin D and anti-resorptives was recorded.

RESULTS: One hundred males and 65 females were receiving oral prednisolone for a mean (SD) duration of 40.4 (29.9) months in males and 41.2 (36.4) months in females. Twenty-one females (12.7%) and 5 (3%) males had bone mineral density measured by DEXA. Of those, 10 (47.6%) females and 3 (50%) males were osteoporotic and 11(52.4%) females and 2 (40%) males were osteopenic. Calcium and vitamin D were prescribed to the majority of patients (60% to 80%), but none were prescribed antiresorptive/anabolic therapy.

CONCLUSIONS: Patients in this study were neither investigated properly nor treated according to the minimum recommendations for the management of GIOP. Physician awareness about the prevention and treatment of GIOP should be a priority for the local health care system.

Osteoporosis is a major public health problem worldwide, with increased morbidity and mortality due to its complications.[1] Postmenopausal osteoporosis has attained the status of a major epidemic and most women with it present with a fracture as the first indication of the disease.[2] In the USA, osteoporosis and the treatment of osteoporosis-related fractures costs are estimated to be in excess of $18 billion a year.[2-3] Bubshait and Sadat-Ali[4] estimated the yearly cost of treating osteoporosis-related femoral fractures in Saudi Arabia as SAR4.27 billion a year. Proper interventions could reduce this cost tremendously.

Glucocorticoids are considered an important component of therapy for a variety of medical conditions including autoimmune, rheumatic, pulmonary and gastrointestinal disorders. Patients treated with glucocorticoids are at risk for many adverse complications.[5] One of the most important complications associated with long-term use of glucocorticoids is glucocorticoid-induced osteoporosis (GIOP).[6,7] Prolonged use of glucocorticoids causes osteocyte apoptosis with an increase in bone resorption and a decrease in bone formation at both the local and systemic levels, leading to rapid weakening of bone architecture and an increase in fracture risk.[8,9] Evidence indicates that GIOP is the most common cause of secondary osteoporosis, leading to fractures in 30% to 50% of patients taking chronic glucocorticoids.[10] However, studies showed that many patients treated with glucocorticoids are not properly evaluated and do not receive prophylaxis or treatment to prevent bone loss.[11,12]

Osteoporosis secondary to sickle cell disease[13] and cancer chemotherapy[14] were reported among the Saudi Arab population. A review of the medical literature found no studies on GIOP in Saudis. We hypothesized that evaluation and management of GIOP at our institution is below the standards. This study was carried out to answer the following questions: 1) To what extent is DEXA scanning performed for patients taking glucocorticoids? 2) What percentage of patients taking long-term glucocorticoids are simultaneously prescribed medications to prevent or treat GIOP?

METHODS

This retrospective study was approved by the research committee of King Faisal University and was carried out at King Fahd Hospital of the University, Al Khobar. We used the local electronic pharmacy prescription monitoring system to identify patients older than 18 years of age, who were prescribed ≥ 7.5 mg of prednisolone per day for 6 months or longer during the period 1 July 2007 through 31 December 2007. Patients who were prescribed other glucocorticoids apart from oral prednisolone or who took the steroids intermittently were not included in the study. Subsequently, each patient chart was reviewed for clinical data including age, sex, dose and duration of glucocorticoids therapy. A mean prednisolone dose was taken for patients receiving the minimum daily dose of ≥ 7.5 milligrams or more for the 6-month period. Dual-energy x-ray absorptiometry (DEXA) scan imaging reports were reviewed when available and data on BMD, T-score and Z-score were documented. Patients with a T score of ≤ 2.5 SD were defined as osteoporotic and those between -1 to -2.5 SD were defined as osteopenic for analysis, as defined per the WHO criteria.[16] Patients who had a DEXA scan were divided into those younger than the age of 35 years, as they had achieved peak bone mass (PBM), and 35 years of age or older. The patient was considered to be screened if he had a BMD measurement while taking glucocorticoid therapy. The concomitant use of osteoporosis prophylaxis or treatment such as calcium, vitamin D, bisphosphonate, calcitonin, and hormonal therapy were noted.

Table 1. Primary diseases in patients (n=165) receiving ≥7.5 mg oral prednisolone daily for 6 months or longer.

Primary disease	Number (%)
Asthma	22 (13.3)
Inflammatory bowel disease	15 (9)
Idiopathic thrombocytopenic purpura	13 (7.9)
Chronic nephritis	16 (9.7)
Neuropathies	5 (3)
Rheumatoid arthritis	45 (27.3)
Renal transplant	33 (20)
Systemic lupus erythematosus	16 (9.8)

Table 2. Prednisolone therapy and anti-osteoporotic prevention and treatment in 165 patients receiving daily prednisolone for 6 months or longer.

	Male (n=100)	Female (n=65)	*P* (males vs. females)
Mean (SD) dose and range of prednisolone (mg)	15.9 (12.7) (7.5-60)	21.5 (19.5) (7.5-100)	.05
Mean (SD) duration and range of prednisolone (mo)	40.4 (29.9) (6-108)	41.2 (36.4) (6-121)	.2
Treatment with calcium	81 (81%)	40 (61.5%)	.05
Treatment with vitamin D	71 (71%)	38 (58.5%)	.1
Antiresorptives/anabolics	0	0	

Data was analyzed using a *t* test to compare means between the non-osteoporotic, osteopenic and osteoporotic patients. All tests were performed using SPSS (Statistical Package for the Social Sciences), version 14.0, Chicago, Illinois[15] a *P* value of <.05 considered statistically significant.

RESULTS

During the period 1 July 2007 through 31 December 2007, 516 patients received oral corticosteroid therapy according to the local electronic pharmacy prescription monitoring system. One hundred and sixty-five patients (32.0%) received ≥ 7.5 mg of oral prednisolone per day for 6 months are longer, including 100 males and 65 female patients with a mean (SD) age and range of 37 (12.7) years (range, 7.5-60 years) for males and 40.8 (15) years (range, 18-62 years) for females (Tables 1, 2). Only 26 patients (15.8%) had BMD measured by DEXA scan, including 21 females (32.2% of females) and 5 males (5.0% of males) (P=.001) of whom 10 females and 3 males were osteoporotic and 11 females and 2 males were osteopenic (Table 3). None of the patients who had a DEXA scan during glucocorticoid therapy had normal BMD. Fourteen patients were <35 years and 12 were >35 years. In the former group, 10 (71.5%) were osteoporotic compared to 5 (42%) in the latter group. Calcium supplementation was prescribed for 81 (81.0%) males compared to 40 (61.5%) females (P=.05). There was no significant difference in the frequency of prescription of vitamin D supplementation between males and females. None of the 165 patients who received ≥ 7.5

milligrams of steroids daily for 6 months or longer were receiving anti-resorptive/anabolic drugs as prophylaxis or therapy for osteoporosis.

DISCUSSION

Secondary osteoporosis is common but still neglected. It is the cause for osteoporosis in almost two-thirds of males, more than half of pre-menopaual and peri-menopausal females, and about one-fifth of post-menopausal females.[16] Etiologies of secondary osteoporosis are many; however, GIOP is one of the leading causes. GIOP and its risk of fragility fractures are well recognized. The combined effect of higher dose, longer duration and a continuous pattern of glucocorticoid therapy could increase vertebral fracture risk by 17-fold and hip fracture risk by 7-fold.[17,18] For this reason, many international guidelines regarding evaluation and treatment of GIOP have been developed. Those guidelines indicate that the use of more ≥5 milligrams for 3 months or longer warrant a DEXA scan to diagnose boss loss and to start prophylactic anti-resorptive therapy using a bisphosphonate or other drugs to prevent osteoporosis.[19-22]

Our study showed that during a 6-month period a total of 516 patients were receiving oral predinisolone and 165 patients (32%) were taking ≥7.5 milligrams of steroid per day for 6 months or longer. According to international guidelines, all patients in the later group should have been screened and received effective prophylaxis or therapy for osteoporosis. Despite the fact that we used a higher dose and longer duration of therapy (≥7.5 milligrams for ≥6 months) than what is recommended in recent guidelines,[19,20] only 26 (15.8%) of our patients were evaluated by DEXA scan and all of them had either osteopenia or osteoporosis. A DEXA scan was ordered for only 5 of 100 men. This indicates that physicians are less concerned about the development of osteoporosis in male patients despite the fact that men older than the age of 50 years were found by our group to have osteoporosis of the hip in 24.3% and osteoporosis of the spine in 37.4% in a previous study.[23] The majority of our patients were taking calcium and vitamin D supplements, which is a higher rate than in other studies,[24] but unfortunately, none of our patients, including those who were documented to have low bone mass, were prescribed bisphosphonates or any other anti-resorptive or anabolic therapy to prevent or treat osteoporosis. Neglect in providing adequate and recommended prophylaxis or therapy for patients on long-term glucocorticoids appears to be universal. In the study of Gudbjornsson et al (2002),[12] only 9% of patients were taking a bisphosphonate.

Table 3. Clinical characteristics of 26 patients who had bone mineral density measured by DEXA scan.

	Male (n=5)	Female (n=21)
Mean (SD) age (years)	50 (17.4)	36.5 (12.1)
Osteopenia (n)	3	11
Osteoporosis (n)	2	10
Mean (SD) spine BMD (g/cm^2)	0.707 (0.12)	0.783 (0.16)
T score (spine)	-3.2 (0.96)	-2.2 (0.9)
Z score (spine)	-2.24 (0.69)	-1.81 (0.89)
Mean (SD) hip BMD (g/m^2)	0.632 (0.13)	0.680 (0.15)
T score (hip)	-2.24 (1.03)	-2.04 (0.65)
Z score (hip)	-1.44 (0.68)	-1.45 (0.78)

Hart and Green (2002)[25] found that 64.7% of their patients did not receive the proper prophylaxis for GIOP. Ungprasert et al (2007)[26] believed that neglect by internal medicine physicians is quite common even in teaching institutions, as in their hospital only 5.8% of patients were evaluated for GIOP while Guzman-Clark and associates (2007)[24] found that the common barrier for GIOP management was the physician lack of awareness and knowledge.

The mean age of our patients was lower than that reported in other studies.[12,23] This could have been due to different disease patterns and different indications for glucocorticoid therapy. This might also explain the difference in the mean glucocorticoid dose between men and women. In this study we did not evaluate the reasons for steroid therapy or the specialty of the prescribing physicians. Another important finding of our study was the higher incidence of low bone mass in patients who are younger than 35 years of age, which may indicate that patients at a younger age who have not attained PBM are at greater risk of developing GIOP.

Our study has several shortcomings including all those associated with being retrospective. In addition, we did not have vitamin D levels and bone markers available for analysis. Lastly, we did not evaluate the indications of glucocorticoid therapy, which can be a contributing factor to low bone mass.

In conclusion, this study shows that GIOP is neither diagnosed early nor properly managed at our teaching institution. The fact that none of our patients who were on long-term glucocorticoid therapy had been prescribed anti-resorptive drugs raises a concern about the lack of knowledge of international guidelines regarding GIOP. Awareness programs appear to be urgently needed for the physicians prescribing glucocorticoids in order to prevent GIOP and its complications.

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case report

Autologous bone marrow transplanation for extramedullary plasmacytoma presenting as adrenal incidentaloma

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Ann Saudi Med 2009; 29(3): 219-222

Extramedullary adrenal plasmacytoma (EMP) involving the adrenal glands is rarely encountered clinically. We report a A 47-year-old male who presented with bilateral adrenal incidentalomas. After confirming EMP, the patient received two consecutive autologous hematopoietic stem cell transplants (HSCT) using high-dose melphalan. Following HSCT, a serial follow-up helical CT revealed a substantial decrease in the size of both adrenal masses. Serial periodic serum protein and urine electrophoresis and immunofixation showed abrogation of a previously noted monoclonal band. At 50 months follow-up the patient was alive and well. Our patient is the first with EMP to have received an autologous HSCT, which may prove to have a role in therapy due to the immunological effect of the infused donor marrow T-lymphocytes against the clonal proliferation of abnormal plasma cells in extrammedullary sites.This case indicates that an EMP should be added to the differential diagnosis of adrenal incidentalomas.

Plasmacytomas are tumors that arise in different locations due to the ubiquitous tissue distribution of plasma cells. They are a clonal proliferation of atypical plasma cells that exhibit a localized osseous or extraosseous (extramedullary) growth pattern.[1] Extramedullary plasmacytomas (EMPs) have been described in a variety of locations.[1] EMP involving the adrenal gland is unusual. In reporting the case, we wish to draw attention to its possibility in the differential diagnosis of adrenal incidentalomas.

CASE

A 47-year-old male presented at an outside hospital with painful right hip that was diagnosed as synovitis of the hip. A CT scan of the hip that included the abdomen detected bilateral adrenal masses. At presentation he was totally asymptomatic and other than large palpable bilateral abdominal flank masses had a totally negative physical examination. The patient underwent the following investigations: hemoglobin 149 g/L, red blood cells 5.37×10^{12}/L, WBC 6.1×10^{9}/L, serum creatinine 87 μmol/L (reference range, 65-129 μmol/L) serum calcium 1.95-2.25 g/L (reference range, 2.10-2.55 g/L), serum albumin 35 g/L (reference range, 42-48 g/L), serum phosphorus 0.57-1.27 mmol/L (reference range, 0.7-1.45 mmol/L), alkaline phosphatase 64-96 U/L (reference range, 40-115 U/L), total proteins 109 g/L (reference range, 65-81 g/L), and urine total protein of 1.22 g/L. The hormonal profile consisted of 24-hour urine normetanephrines of 2.88 μmol/day (reference range, 0-3.43 μmol), urine metanephrines of 0 μmol/day (reference range, 0-1.49), urine 3-methoxytyramine 1.34 μmol/day (reference range, 0-2.06), synthetic ACTH stimulation testing revealed a normal adrenal cortical reserve (base line serum cortisol, 301 nmol/L that increased to a peak of 564.7 nmol/L at one hour following intramuscular administration of 250 μg of 1-24 synthetic ACTH), urine cortisol of 45 μg/day (reference range, <100 μg/day), urine aldosterone <33 nmol/day (reference range, 8-83 nmol/day), supine renin of 2.17 μg/L/h (reference range, 0.15-2.33 μg/L/h), and serum dehydroepiandrosterone sulfate of 0.7 μmol/L (reference range, 1.2-8.71). Imaging data consisted of an ultrasound of the abdomen/pelvis (not shown) that revealed large bilateral adrenal masses, a CT of the abdomen (Figure 1a without contrast and figure 1b following contrast administration) and an MRI abdomen (not shown) that showed massive bilateral adrenal masses, displacing the kidneys inferiorly, but that was otherwise negative. A skeletal survey (ribs, clavicle, scapulae, skull, spine, long bones of upper and lower extremities, pelvis), whole body bone scan and MRI spine showed no findings suggestive of multiple myeloma. Ultrasound-guided fine needle aspiration biopsy of the right adrenal mass (Figure 2a) and a core-needle biopsy (Figure 2b) showed morphological findings consistent with the diagnosis of plasmacytoma. Immunohistochemical staining data (Figures 2c and 2d) supported the diagnosis of plasmacytoma. Flow cytometry analysis of the adrenal tumor revealed an abnormal CD38+ cell population that exhibited monoclonal cytoplasmic kappa light chain expression, but negative for CD45, cytokeratin and lambda light chain (Figure 3). A bone marrow aspirate showed normocellular pattern with no evidence of multiple myeloma. Bone marrow flow cytometry for leukemia/lymphoma markers was negative. A distinct monoclonal protein band accounting for 44.6% of total serum proteins and 87.9% total gamma globulins was shown on serum protein electrophoresis. (Figure 4a) . Immunofixation electrophorisis of urine specimen demonstrated free kappa light chain (Bence Jones proteins) (Figure 4b).

At initial treatment the patient received chemotherapy consisting of two cycles of vincristine, Adriamycin and dexamethasone (VAD) followed by two cycles of etoposide, dexamethasone, Ara-C and cisplatinum (EDAP). A follow-up CT scan showed no change in the size of the bilateral adrenal lesions nor was there a change in the immunological studies of serum and urine. Two years following initial presentation the patient received two consecutive autologous hematopoietic stem cell transplantation (HSCT) procedures using high dose melphalan. Starting 6 months post-HSCT through a last follow-up at 50 months, serial periodic serum protein electrophoresis and immunofixation showed abrogation of a previously noted monoclonal band. Urine electrophoresis and urine immunofixation also turned out to be negative for Bence-Jones proteins. A last CT scan of the abdomen done at 47 month follow-up (Figure 1b) revealed that both adrenal tumors had regressed substantially and demonstrated findings of calcification and fibrosis. A follow-up skeletal survey at 47 months showed normal findings. At 50 months follow-up the patient was alive and well.

DISCUSSION

The diagnosis in our case was based on the findings of a plasma cell tumor in an extramedullary site detected on adrenal imaging, the tissue diagnosis, the relevant immunological analysis of serum and urine, flow cytometry of the adrenal tumor, the absence of mutiple myeloma on bone marrow examination and the absence of skeletal lesions, coupled with the long-term follow-up data. An EMP is a rare malignant tumor. Fewer than 3% of all plasma cell proliferative disorders are EMPs.[2] In the majority of instances (80% of cases), they occur in the upper respiratory tract or the oral cavity.[3] The remainder arise in the gastrointestinal tract, central nervous system, breast, spleen, retroperitoneum, testes, and the thyroid or the lymph nodes.[3]

Extramedullary plasmacytoma involving the adrenal gland is unusual. It has been reported in 4 other cases previously.[3-6] Three of these cases were reported in middle-aged Japenese men presenting as adrenal incidentaloma who had an IgG monoclonal spike that was characterized as lambda light chain on immunoelectrophoresis.[3-5] In previously reported cases the adrenal plasmacytomas were all unilateral right-sided lesions and compared to our case were relatively smaller in size (3.5-4 cm).[3-6] All were hormonally non-functioning[3-6] as was our case and their follow-up data extended up to a year. Fujikata et al have reported no tumor recurrence after a year of follow-up following surgical excision and radiotherapy.[5] Laproscopic adrenalectomy was done in 3 other cases reported by Kahara et al,[3] Asahi et al,[4] and Rogers et al.[6]

In contrast to previously reported cases, our case is dintinct in presenting with bilateral incidentalomas that were much larger, producing IgG kappa light chain, followed-up for a longer time period without surgical intervention but received chemotherapy that was considered a failure and had then undergone two consecutive autologous HSCT procedures. Following the first HSCT patient demonstrated a partial reduction of the adrenal masses and an improvement in protein electrophoresis. Considering these responses, a second HSCT procedure was undertaken that was temporally related to a significant reduction in the tumor size and resolution of the abnormal findings in serum and urine electrophoresis. These responses remained sustained without maintenance therapy. Because a biopsy was not performed from the contralateral left adrenal mass, we cannot definitely state that our patient indeed had bilateral plasmacytomas. However, the imaging findings, the follow-up data and the regression in the size similar to that of the right adrenal plasmacytoma following HSCT is highly suggestive of a bilateral process.

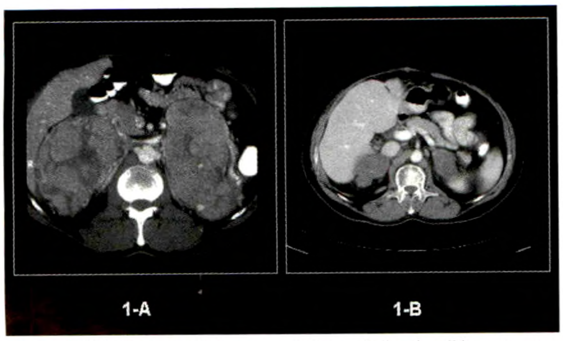

Figure 1. (A) CT scan abdomen, axial view following IV contrast administration (at presentation) revealed bilateral adrenal tumors with heterogeneous enhancement. The right adrenal tumor measured 11×8 cm while the left one measured 13×8 cm. Prominent vessels are demonstrated around the masses. Note the clear lobulations seperated by hypodense linear areas of probable fibrosis and necrosis within the tumor masses. (B) An axial contrast-enhanced CT image through the adrenals performed 47 months follow-up demonstrated marked interval decrease in both size and enhancement of bilateral adrenal masses.The right adrenal tumotr had decreased substantially to 5.2×4×5.7 cm and the left adrenal mass is regressed to 4.5×5×3.5 cm and showed findings of calcification and findings suggestive of fibrosis.

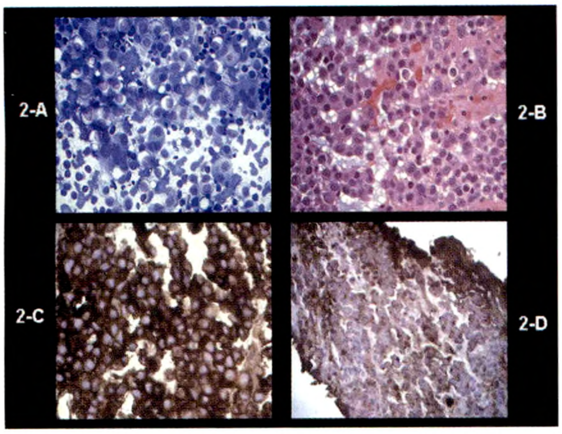

Figure 2. (A) Photomicrograph of the FNA biopsy specimen from right adrenal tumor showing clusters of plasma cells with eccentric nuclei, and prominent nucleoli; some of these cells show bi- and multi-nucleation (Diff Quick stain, ×400). (B) Photomicrograph of the biopsy specimen shows similar findings (hematoxylin and eosin stain, ×400). (C) Photomicrograph of the biopsy specimen from the adrenal tumor demonstrates plasma cells strongly positive for Kappa light chain (paraffin section, immunoperoxidase staining, ×400). (D) Photomicrograph of the biopsy specimen from the adrenal tumor shows strong staining of plasma cells with antibody to CD 38 (paraffin section, immunoperoxidase staining, ×400).

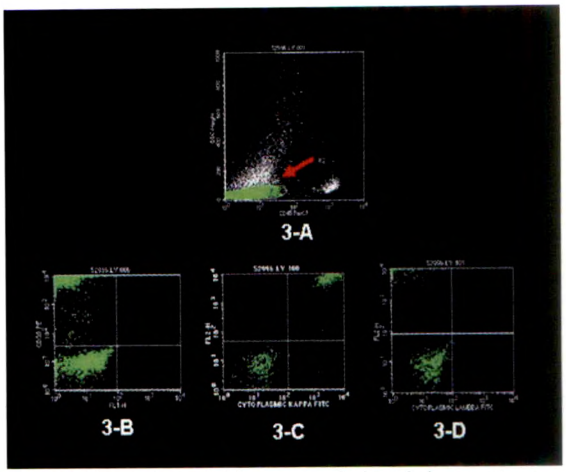

Figure 3. Flow cytometric histograms of adrenal plasmacytoma. Note the dim CD45 gate on upper panel (arrow) (A). Immunophenotyping revealed the monoclonal cytoplasmic kappa light chain expression in the CD38+ cells after permealization (3 bottom panels B-D).

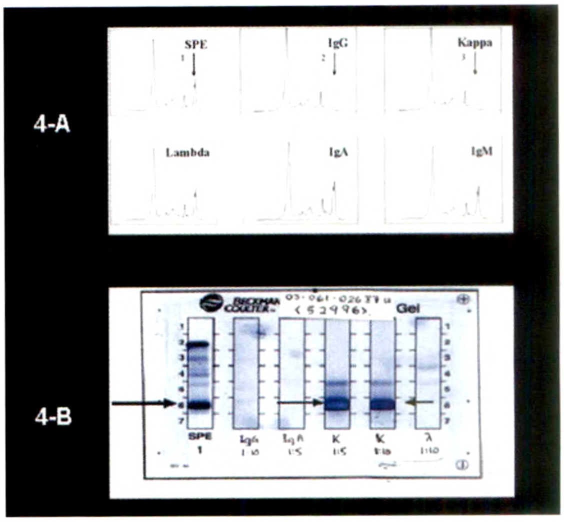

Figure 4. (A) Monoclonal protein typing by immunosubtraction on capillary zone electrophoresis (CZE). Note the distinct monoclonal protein peak (1) on CZE-SPE in the γ region, that is removed from the electrophoresis pattern by antisera to gamma (2) heavy chains (anti-IgG) and kappa light chains (3). The antisera to IgG lambda, IgA, and IgM had no effect (lower panel). The immunosubtraction indicated the monoclonal protein is IgG Kappa. (B) Immunofixation electrophoresis (IFE) of urine specimen for Bence-Jones protein (BJP) using Beckman Paragon system. Note the dense band of free kappa light chains corresponding to the band seen on urine protein electrophoresis (UPE). Note also the prozone effect (antigen excess) using 1:5 dilution, and its disappearance using 1:10 dilution.

The role of HSCT in the management of EMPs is not defined. For the last 20 years autologus and allogeneic HSCT have been used to advantage in patients with multiple myeloma.[7,8] However, there is no previous experience whatsoever regarding the use of HSCT in the management of adrenal plasmacytoma. Our patient with extramedullary plasmacytoma of the adrenal is the first to have received an autologous HSCT. HSCT may have a potential role, probably due to an immunological effect of the infused donor's marrow T-lymphocytes against the clonal proliferation of abnormal plasma cells in extrammedullary sites. We remain cautiously optimistic on the impact of consecutive autologous HSCT in EMP in our patient. Unquestionably, more experience is needed to study the effect of HSCT in extramedullary EMPs in general.

In conclusion, although the frequency of diagnosis of adrenal incidentaloma has increased with the increased use of contemporary imaging modalities, the definitive diagnosis of such lesions should rest on a combination of clinical and pertinent laboratory criteria coupled with cytological/histological criteria. Thorough investigations will lead to the diagnosis of most unusual adrenal lesions, which can have an enormous impact on treatment, quality of life and on eventual outcome. EMP should be considered among the differential diagnoses of adrenal incidentalomas.

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case report

Gastrointestinal angiodysplasia in three Saudi children

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Ann Saudi Med 2009; 29(3): 223-226

Angiodysplasia is a term used to describe distinct gastrointestinal mucosal ectasias that are not associated with cutaneous lesions, systemic vascular disease or a familial syndrome. Seventy-seven percent of angiodysplasia are located in the cecum and/or ascending colon. Fifteen percent are located in the jejunum and/or ileum and the remainder are distributed throughout the alimentary tract. Most commonly, the angiodysplastic lesions are typically seen in elderly patients of both genders, although gastric and duodenal lesions have been reported occasionally in subjects within the third decade of life. However, data on infants and children are scarce. We describe three cases (ages 7 days, 2 years, and 5 years) who presented to our unit with gastrointestinal bleeding. One of these patients developed moderate-to-severe symptoms and was blood-transfusion dependent. She was misdiagnosed as having inflammatory bowel disease and underwent a total colectomy and ileoanal anastomosis. The other two patients were managed conservatively for up to 5 years with no further bleeding.

Angiodysplasia is the term used to describe distinct gastrointestinal mucosal vascular ectasias that are not associated with cutaneous lesions, systemic vascular disease or a familial syndrome. These lesions may be flat, red spots (2-5 mm) or slightly raised. The lesions have many similarities to those of the telangiectasias, but angiodysplasia is not a component of a systemic, metabolic or hereditary disease with other manifestations.[1] Seventy-seven percent of angiodysplasias are located in the cecum and/or ascending colon. Fifteen percent are located in the jejunum and/or ileum and the remainder are distributed throughout the alimentary tract.[2] The exact cause of angiodysplasias is unknown, but the widely accepted theory is that they are related to degenerative changes of the small blood vessels associated with aging. Other theories include long-term local hypo-oxygenation of the microcirculation from cardiac, vascular or pulmonary disease.[1] Mucosal hypoperfusion from cardiac disease was postulated to be the underlying cause for development of angiodysplasia, but echocardiogram studies indicated that only a few patients with angiodysplastic lesions had significant valvular heart disease such as aortic stenosis.[2] In many instances angiodysplasia disappear following aortic valve replacement.[3] Roskell et al demonstrated a relative deficiency of collagen type IV in mucosal vessels in angiodysplasia compared with controls.[4] Angiodysplasia has been reported in adults, but data on infants and children are scarce. We describe three cases that presented to our pediatric gastroenterology unit.

CASE 1

The first case was a 5-year-old Saudi female who had severe, frequent bloody diarrhea for two years associated with intermittent abdominal pain, poor appetite and failure to gain weight. At age of 3 years, she was treated at her local hospital for amoebic dysentery with antibiotics (sulfamethoxazole-trimethoprim and metronidazole) with no obvious improvement, followed by eliminating dietary milk products with some improvement, but she later had a recurrence of symptoms. Sigmoidoscopy in the local hospital showed a normal looking mucosa and biopsies showed chronic nonspecific colitis; subsequently, the patient was started on prednisolone empirically with good response, but whenever the steroid dose was tapered, she started to bleed again from the rectum. She was referred to our center as having steroid-dependent colitis for further management. Examination revealed a pale, non-thriving child with both weight and height below the fifth percentile for age. The rest of the systemic examination was normal. Her hemoglobin was 5.3 mg/dL (normal, 11.0-14.0 mg/dL), mean corpuscular volume was 64.1 fL (normal, 80.0-94.0 fL), mean corpuscular hemoglobin was 19.9 pg/cell (normal, 27.0-32.0 pg/cell), the erythrocyte sedimentation rate was 31 mm/h, and stool for occult blood was positive, serum albumin was 38 g/L (normal, 32-46 g/L), and total protein was 69 g/L (normal 65-81 g/L). Colonoscopy revealed tiny angiodysplastic lesions in the rectum, sigmoid colon, and the ascending colon (Figure 1). The transverse colon and cecum again showed small hemorrhagic angiodysplastic lesions with typical fold processes of dilated superficial mucosal capillaries. No ulcers or erosions were seen (Figure 2). The upper gastrointestinal endoscopy was normal. The steroid was tapered and stopped. She became blood transfusion-dependent, requiring one transfusion every 3 to 4 weeks. With involvement of the whole colon with angiodysplastic lesions, a normal upper gastrointestinal endoscopy and with moderate-to-severe symptoms requiring multiple blood transfusion, the patient underwent total colectomy and ileo-anal anastomosis with a smooth post-operative course. Histological examination was consistent with angiodysplastic lesions in different parts of the colon (Figure 3). Follow-up in the clinic up to 3 years post-surgery showed that the patient had no more rectal bleeding. Her growth improved and her hemoglobin stabilized at >10 mg/dL.

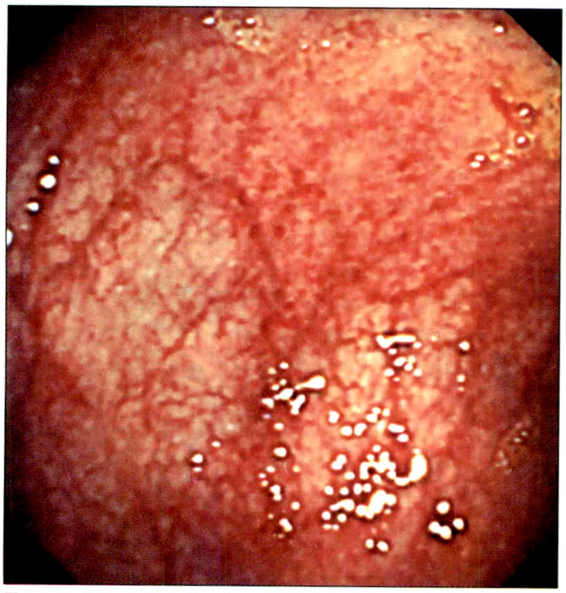

Figure 1. Diffuse bleeding form tiny angiodysplastic lesions over the sigmoid colon.

CASE 2

A 2-year-old male was admitted at 5 months of age with fever and bronchopneumonia. He was treated with antibiotics and improved. Two weeks post-discharge, the infant developed hematemesis and melena. He was hemodynamically stable with a hemoglobin of 6.2 mg/dL (normal, 11.0-14.0 mg/dL) and needed blood transfusion. The liver and renal function tests were unremarkable. Upper gastrointestinal endoscopy in a local hospital revealed angiodysplasia at the greater curvature of the stomach with some oozing points. There were no esophageal varices and no ulcers. He was referred to our center with recurrent hematemesis for further management. At the age of 1 year, upper GI endoscopy at our center revealed a normal esophagus with few angiodysplastic lesions over the body of the stomach while the duodenum was normal. Colonoscopy showed dilated blood vessels consistent with angiodysplastic lesions from the rectum to the mid-ascending colon. He was treated conservatively, without surgical intervention. He had no further bleeding and was placed on iron therapy. At the age of 6 years, he was seen in the clinic and had a weight and height above the tenth percentile. His hemoglobin was 13.3 mg/dL while maintained on an iron supplement.

CASE 3

A 7-day-old male infant, a product of a full-term in vitro fertilization pregnancy was delivered by lower segment cesarean delivery secondary to fetal distress by a mother with primary infertility for six years. The baby was dusky after birth and was resuscitated with oxygen using an Ambu bag, but did not need intubation to resolve transient tachypnea of the newborn. He was fed with artificial feeds (cow's milk formula). On day 3, he had a bloody stool, with no abdominal distension and audible bowel sounds. He did not appear septic and vital signs were normal. He was placed on nil per OS nothing by mouth status and started on intravenous ampicillin and gentamicin after appropriate cultures were taken. An abdominal x-ray was unremarkable. His complete blood count, including platelet count and coagulation profiles were normal. Stools on day 6, 7 and 8 were positive for occult blood. He underwent colonoscopy on day 8, which revealed angiodysplastic lesions oozing blood. The lesions increased in number as the scope advanced proximally to the sigmoid and descending colon and decreased toward the transverse and ascending colon. Bleeding appeared whenever air or water were applied directly over the lesions. The mother refused upper GI endoscopy for evaluation of the rest of the gut. The patient was treated with oral iron supple-

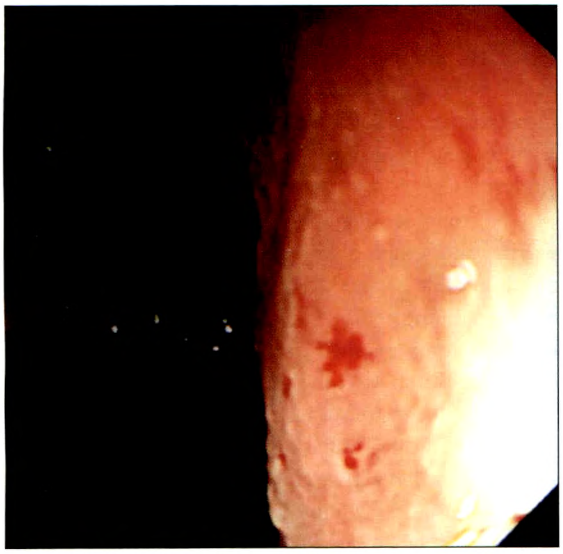

Figure 2. Typical fold processes of dilated superficial mucosal capillaries in the sigmoid colon.

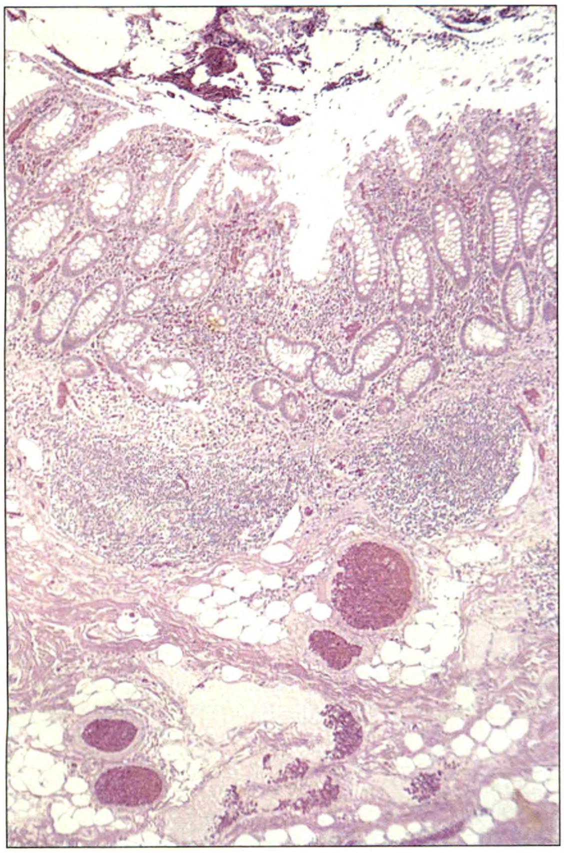

Figure 3. Colonic surgical specimen showing angiodysplastic lesions.

mentation and discharged home. On follow-up, he had no more bleeding and received iron therapy as needed. At 3 years of follow-up, the baby was growing well with no rectal bleeding and had a stable hemoglobin of 11 mg/dL.

DISCUSSION

Angiodysplasia is an increasingly recognized disorder in adults and the prevalence appears higher than was originally suspected.[5] Among adults, angiodysplasia of the stomach or duodenum was found in 1% to 2% of 25 consecutive subjects undergoing upper gastrointestinal endoscopy for a variety of indications.[5] Angiodysplasia is found during colonoscopy at slightly higher rate of 3% to 6% of subjects undergoing the procedure for a variety of indications.[6,7] Angiodysplasia can be an incidental finding in nearly half of the cases in which it is detected.[6] Most commonly, the angiodysplastic lesions are typically seen in elderly patients of both genders, although gastric and duodenal lesions occasionally have been reported in subjects during the third decade of life.[5,8] Data are scarce in infants and children, and to our knowledge, these are the first case reports among Saudi children. As with upper tract lesions, very young subjects with colonic angiodysplasia have also been described.[9] Angiodysplasia may present with maroon-colored stool, melena, and hematochasia as in Case 1 and 3 or hematenesis as in Case 2. In 10% to 15% of patients, iron deficiency anemia is observed and stools are intermittently positive for occult blood (as in Case 2 and 3).[6] Fifteen percent of patients present with massive hemorrhage as in Case 1, and bleeding stops spontaneously in more than 90% of cases (as in Case 2 and 3).[7] While there are many modalities for diagnosis of angiodysplasia such as selective mesenteric angiography, 99m Tc-labeled red blood cells, 99m Tc-labeled sulfur colloid, CT angiography, air contrast enema and wireless capsule, colonoscopy is the most common method of diagnosis as well as therapy. The sensitivity of colonoscopy exceeds 80% when the lesions are located in the area examined by colonoscopy.[7]

In Case 1, a limited sigmoidoscopy was performed and she was misdiagnosed as having inflammatory bowel disease. Endoscopic forceps biopsy has revealed characteristic histopathological features of angiodysplasia in only 31% to 60% of specimens.[10] Angiodysplasia is infrequently detected by visual inspection of the serosal side of the bowel wall.[11] In 1 of 39 adult cases (2.6%), the diagnosis was made during surgical exploration, and 14 (35.8%) of these individuals underwent 21 non-diagnostic surgeries prior to their evaluation. A conservative approach to hemodynamically stable patients is recommended as bleeding ceases spontaneously in the majority of the cases (as in Case 2 and 3). Gastric and duodenal angiodysplastic lesions are managed with endoscopic obliteration techniques. In one study, the blood replacement requirements for a group of 13 patients decreased by 50% with 4 patients requiring no further transfusion.[12] Endoscopic laser photocoagulation is a successful modality in controlling bleeding from colonic angiodysplasia. However, complications occur in as many as 15% and are more common when the Nd: Yag Laser (neodymium-doped yttrium aluminium garnet; Nd:Y3Al5O12) is used in the right colon.[10] In a pilot study, 14 patients bleeding from angiodysplasia and 4 bleeding from Dieulafoy lesions located in the small bowel observed that endoscopic band ligation achieved hemostasis in a single session in all patients.[13]

Angiodysplasia that presents with acute hemorrhage can be effectively controlled with embolization, although it is seldom needed, as in our three cases. Selective infusion of vasopressin is less effective than embolization because of a higher bleeding rate. However, intra-arterial vasopressin can control massive lower gastrointestinal bleeding in 70% to 91% of patients, but bleeding recurs after discontinuation of vasopressin in 22% to 71% of patients.[10] Octreotide treatment should be considered in patients with refractory gastrointestinal bleeding due to angiodysplasia, in particular in those who need anticoagulant treatment.[14] Octerotide has shown a beneficial response in the long-term management of patients with gastrointestinal angiodysplasia.[15,16]

Colectomy for angiodysplasia is a second-line therapy after endoscopic ablation if endoscopic therapies are not applicable as was the case in our first case, and if life-threatening hemorrhage occurs. In one report, right hemicolectomy resulted in 63% of subjects remaining free of intestinal bleeding for a mean of 3.6 years, and 37% had some degree of recurrent bleeding.[12] Re-bleeding after hemicolectomies occurs in 5% to 30%,[13] which is much less than with endoscopy technique. In general, the prognosis is favorable because most angiodysplasias spontaneously cease bleeding in more than 90% of cases,[16] as in Cases 2 and 3.

In summary, gastrointestinal angiodysplasia is a rare disorder seen in infants and children. In the majority of cases, bleeding stops spontaneously and no further treatment is required. A minority of cases present with moderate-to-severe symptoms needing frequent blood transfusions, and endoscopic and/or surgical intervention may be inevitable.

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Neonatal familial Evans syndrome associated with joint hypermobility and mitral valve regurgitation in three siblings in a Saudi Arab family

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Accepted for publication October 2008

Ann Saudi Med 2009; 29(3): 227-230

The occurrence of autoimmune hemolytic anemia and immune thrombocytopenia in the absence of a known underlying cause led to the diagnosis of Evans syndrome in a 9-month-old male. Subsequently, a similar diagnosis was made in two siblings (a 3-year-old boy and a 1-day-old girl). The 9-month-old had a chronic course with exacerbations. He was treated with steroids, intravenous immunoglobulin and colchicine with a variable response. He died of congestive heart failure at the age of 8 years. The brother's disease course was one of remission and exacerbation. With time, remissions were prolonged and paralleled an improvement in joint hypermobility. The sister died of sepsis after a chronic course with severe exacerbations. Only two families with Evans syndrome have been reported in the English medical literature. In one report (in a Saudi Arab family), the disease was associated with hereditary spastic paraplegia.

Evans syndrome is the occurrence of a Coombs positive hemolytic anemia and immune thrombocytopenia without a known underlying etiology.[1] It is a chronic immunological disorder with a variable course, and the exact pathophysiology is unknown.[2] The disease can present in the neonatal period.3 There are rare reports of familial Evans syndrome.[4,5] Joint hypermobility, not a disease in itself, is defined as an abnormally increased range of joint motion due to excessive laxity of the constraining soft tissues. Hypermobility is determined according to the criteria of Beighton et al.[6] Patients are given a score of 0-9, one point being allocated for the ability to perform each of the tests: 1) passive dorsiflexion of the little finger beyond 90°; 2) passive apposition of the thumb to the flexor aspects of the forearm; 3) hyperextension of the elbow beyond 10°; 4) hyperextension of the knee beyond 10°; and 5) forward flexion of the trunk, with the knees straight, so the palms of the hands rest easily on the floor. Patients are considered hypermobile if they score 4 or more out of 9.

Hypermobility may be a benign syndrome or part of a genetic disorder like Ehlers-Danlos syndrome or Marfan syndrome. All have strong genetic components.[7-9] The benign type is commonly inherited as an autosomal dominant, although autosomal recessive and X-linked transmission also have been documented.[9] We describe three siblings with Evans syndrome, generalized joint hypermobility, and mitral valve prolapse causing mitral regurgitation. The parents of these children are first cousins and have two other children. There was no anemia, thrombocytopenia or joint hypermobility in these other children or their parents. The father is married to another wife, a first cousin as well, with five children. The children and their mother are free of anemia, thrombocytopenia and joint hypermobility.

CASE 1

A full-term Saudi male infant, a product of a first cousin consanguineous marriage, developed jaundice in the first day of life. The mother's blood group was O and Rh negative. The infant's blood group was A positive, and the father's blood group was A positive. Serum bilirubin was 231 µmol/L (reference range, 5-17 µmol/L). Hemoglobin was 130 g/L (reference range, 145-185 g/L), the platelet count was 91×10^9/L (reference range, 150-450×10^9/L) and the direct agglutination test (DAT) was strongly positive. An extended blood group (Kell, Duffy and Kid) showed no minor group incompatibility. He was diagnosed with ABO incompatibility and treated with phototherapy for two days and discharged. He presented in January 1991, at the age of 9 months, with recurrent epistaxis and petechiae of 3 months' duration. He was pale, jaundiced, with multiple petechiae and generalized joint hypermobility (Beighton score of 8/9). There was clinical evidence of mitral regurgitation. An echocardiogram revealed mitral valve prolapse (MVP) and severe mitral regurgitation. There were no features of known collagen disease or syndromes involving joint hypermobility. Laboratory tests showed a hemoglobin of 51 g/L (reference range, 114-127 g/L), WBC of 3.3×10^9/L (reference range, 6-17.5×10^9/L), a platelet count of 9×10^9/L (reference range, 150-450×10^9/L), a reticulocyte count of 7.6% (reference range, 0-1%) and a positive Coombs test. The bone marrow was hypercellular with an increased number of megakaryocytes. Immune-phenotyping and serum immunoglobulin levels were normal and antinuclear antibodies (ANA) were negative. Antiplatelet antibodies were not obtained. Evans syndrome was diagnosed. He was treated with steroids, intravenous immunoglobulin and colchicine with a variable response. He ran a chronic course with exacerbations. Episodes of epistaxis and petechiae were observed in the presence of a platelet count of 80 to 90×10^9/L with no response to different modalities of treatment. He died, at the age of 8 years, of congestive heart failure secondary to severe mitral regurgitation following chordal rupture, which was confirmed by an echocardiogram while awaiting acceptance to a cardiac center.

CASE 2

A brother of the first patient, this male infant, born at term, had jaundice on the first day of life. Laboratory data showed a serum bilirubin of 211 μmol/L (reference range, 5-17 μmol/L), a hemoglobin of 175 g/L (reference range, 145-185 g/L), white blood count of 9.7×10^9/L (reference range, 9.4-34×10^9/L), a platelet count of 114×10^9/L (reference range,150-450×10^9/L), nucleated red blood cells 14/100 white blood cells (reference range, 0-5 nucleated RBC/100 WBC) and strongly positive DAT. The patient's blood group was O positive and the mother's blood group was O and Rh negative. An extended blood group was not obtained. He was diagnosed as having minor group incompatibility, treated with phototherapy for one day, and discharged. He was lost to follow-up until October 1995 (age 3 years), when he presented with epistaxis and petechiae. He was pale, with petechiae and generalized joint hypermobility (Beighton score 8/9). There was cardiomegaly with a mitral regurgitation murmur. An echocardiogram showed mitral valve prolapse and moderate mitral regurgitation. There were no features indicative of known collagen disorders or other syndromes involving joint hypermobility.

The laboratory data showed WBC of 8.1×10^9/L (reference range, 5.5-15.5×10^9/L), hemoglobin of 83 g/L (reference range, 115-125g/L), a platelet count of 7.0×10^9/L (reference range, 150-450×10^9/L), a reticulocyte count of 6.3% (reference range, 0-2%) and strongly positive DAT. The bone marrow examination revealed many megakaryocytes. Leukocyte phenotype by flow cytometry, cytogenetic studies, immunoglobulin levels and thyroid function were normal. ANA and rheumatoid factor (Rh factor) were negative. DNA analysis was not obtained due to parent refusal. An extended blood group (Kell, Duffy and Kid) showed no minor group incompatibility. Evans syndrome was diagnosed based on the presence of Coombs positive hemolytic anemia and thrombocytopenia. He experienced recurrent and prolonged attacks of epistaxis with a platelet count between 70 and 90×10^9/L. Coagulation screening was normal apart from a prolonged bleeding time (12 minutes) (reference range, 2-7 minutes). He showed variable responses to treatment with steroids and intravenous immunoglobulin. His clinical course was that of remissions and exacerbations. At the time of writing he was in clinical remission for 3 years without treatment. His platelet count was 70-80×10^9/L and he had no further episodes of epistaxis. His joint hypermobility improved (Beighton score=4/9). The mitral valve regurgitation murmur disappeared clinically, but a mild regurgitation was found on an echocardiogram. This coincided with improvement in Beighton score and bleeding episodes.

CASE 3

The 1-day-old sister of the first two cases had jaundice when first seen in October 2002. Clinical examination showed generalized joint hypermobility (Beighton score 8/9) and mitral regurgitation murmur. Laboratory data showed a hemoglobin of 131 g/L (reference range, 145-185 g/L), a leukocyte count of 7.3×10^9/L (reference range, 9.4-34.0×10^9/L), a platelet count of 91×10^9/L (reference range, 150-450×10^9/L) and a normal reticulocyte count. The infant's blood group was A positive with a positive DAT. An extended blood group (Kell, Duffy and Kid) showed no minor group incompatibility. She was diagnosed as having Evans syndrome, treated with phototherapy for 3 days, and discharged. At 18 months of age, she presented with epistaxis. She was clinically pale, jaundiced, with generalized petechiae. The Beighton joint score was unchanged (8/9). Mitral valve prolapse with moderate regurgitation was diagnosed and confirmed by an echocardiogram. There were no symptoms or signs indicating known collagen disorder or other syndromes involving joint hypermobility. Her laboratory data showed a hemoglobin of 71 g/L (reference range, 105-125 g/L), leukocyte count of 3.8×10^9/L (reference range, 6.0-17.0×10^9/L), a platelet count of 7.1×10^9/L (reference range, 150-450×10^9/L), total serum bilirubin 131 µmol/L (reference range, 5-17 µmol/L) and the reticulocyte count was 7.4% (reference range, 0-2%). DAT was positive. Serum immunoglobulin level and leukocyte phenotype by flow cytometry were normal. An HIV test and ANA were negative, and a coagulation screen was normal except the bleeding time, which was prolonged (11.5 minutes) (reference range, 2-7 minutes). The bleeding time remained prolonged even when the platelet count was more than 100×10^9/L. DNA analysis was not obtained due to parent refusal. She responded initially to intravenous methylprednisolone and intravenous immunoglobulin, but then ran a chronic course with exacerbation. She had a mitral valve repair, for congestive cardiac failure, with no significant bleeding. Postoperatively, she entered a chronic severe intravascular hemolytic course, which was refractory to different modalities of treatment including cyclosporine, intermediate doses of cyclophosphamide and infliximab. She died of Pseudomonas septicemia at 33 months of age.

DISCUSSION

Neonatal Evans syndrome, reported once in the literature,[3] developed in three consecutive siblings over an 11-year period. All had jaundice, thrombocytopenia and a positive DAT on the first day of life. In the first patient, neonatal Evans syndrome was not considered because he was thought to have a combination of an ABO incompatibility (the mother's blood group was "O" and the baby's blood group was "A") and rhesus isoimmunization (the mother was Rh negative and the baby was Rh positive). In retrospect, the absence of Rh antibodies in the mother excluded Rh incompatibility, and the presence of thrombocytopenia and strongly positive DAT favors Evans syndrome rather than ABO incompatibility. In the second patient, minor group incompatibility was a diagnosis of exclusion, as an extended blood group was not obtained in the neonatal period. However, the positive DAT at the age of three years can not be due to minor group incompatibility even if it was present. The normal serum immunoglobulin and the negative ANA made immune deficiency and SLE, respectively, unlikely. In the third patient, the diagnosis of Evans syndrome was made easy by the family history.

There are two reports of familial Evans syndrome in the English literature. McLeod et al reported Evans syndrome in three siblings who had no other inherited disorder.[5] We reported two brothers, a product of a first-cousin marriage, with Evans syndrome and an autosomal recessive hereditary spastic paraplegia.[4] The addition of this family further supports a genetic predisposition, most likely an autosomal recessive inheritance pattern, in some cases of Evans syndrome.

The clinical course of multiple recurrences and the use of multiple treatment modalities to control the disease are consistent with reported results by Matthew et al.[10] However, our patients manifested attacks of epistaxis and petechiae out of proportion to their platelet count. Mild bleeding associated with an increased capillary fragility was reported in several genetic collagen disorders.[11] Prolonged bleeding has also been reported in patients with hyperflexible thumbs (one of the diagnostic criteria of joint hypermobility).[12] The latter might explain the prolonged bleeding episodes and bleeding time despite near normal platelets count observed in the third case. The lack of significant bleeding during and after cardiac surgery does not exclude this possibility, as a prolonged bleeding time does not predict a bleeding risk.[13] This is important to realize when Evans syndrome occurs in patients with joint hypermobility, otherwise, the bleeding tendency might be attributed to thrombocytopenia while it is not. This recognition might save the patient from being subject to further treatment.

Generalized joint hypermobility, measured according to Beighton criteria, was present in all patients. The lack of features suggestive of the serious genetic syndrome, and the significant reduction that occurred in Beighton score in the second case as he grew older suggests the benign form of joint hypermobility. The presence of joint hypermobility in the third case, a girl, excludes an X-linked transmission. The lack of joint hypermobility in the parents, who are first cousins, favors an autosomal recessive mode of inheritance in this family.

Deficiency and haploinsuffiency of tenascin-X, a large extracellular glycoprotein, has been identified as a cause of joint hypermobility in patients with benign joint hypermobility syndrome and the mobility type-Ehlers-Danlos syndrome.[14] Tenascin-X forms a genetic unit with CYP21B, C4A, and C4B, termed the RCCX module. This region is highly susceptible to recombination events leading to diverse diseases; for example, systemic lupus erythematosus (SLE) is a consequence of C4A deficiency. IgA deficiency is caused by C4B mutation and a deficiency of CYP21B results in congenital adrenal hyperplasia.[14] The development of autoimmune hemolytic anemia and autoimmune thrombocytopenia is not infrequent in patients with selective IgA defiency[15-17] and SLE.[18] Adult patients with SLE were more hypermobile (48%) than a control group (15%).[19] This suggests a pathogenetic relationship between Evans syndrome, not infrequently present with SLE, and joint hypermobility.

In a recent report from Turkey the incidence of joint hypermobility, as judged by Beighton score, was found to be higher in patients with mitral valve prolapse than controls.[20] Our three patients manifested joint hypermobility with mitral valve prolapse and regurgitation.

The expression of mitral valve prolapse is variable within families.[21] Weakness of the valvular and restraining chordal tissue with sudden chordal rupture causing abrupt clinical deterioration is a recognized feature.[21] This was the cause of death in the first patient. Progressive mitral regurgitation causing heart failure, another feature of mitral valve prolapse,[21] developed in the third patient and was treated surgically. The second patient showed an improvement with time, another feature of mitral valve prolapse.[21]

In conclusion, familial Evans syndrome, possibly an autosomal recessive disorder, may be mistaken for alloimmune hemolytic anemia when it presents in the neonatal period. Although the association of Evans syndrome with joint hypermobility (a genetic collagen disorder) may be a coincidence, a pathogenetic relationship needs to be considered.

Acknowledgments
The authors would like to thank Ms. Charito Samson and Ms. Junelyn Mondala for their secretarial work.

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case report

Defecation of a "colon cast" as a rare presentation of acute graft-versus-host disease

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Ann Saudi Med 2009; 29(3): 231-233

Diffuse involvement of the gastrointestinal tract by graft versus host disease (GVHD) is a common complication of allogeneic hematopoietic stem cell transplant (HSCT). Gastrointestinal GVHD usually presents 3 or more weeks after HSCT and is characterized by profuse diarrhea, anorexia, nausea, vomiting, abdominal pain and gastrointestinal bleeding. We report a case of a 23-year-old male who had undergone allogeneic HSCT and presented with bloody diarrhea on the 90th day post-HSCT. On the fourth day of admission, the patient passed per rectum a 27-cm long pinkish colored fleshy material recognized as a "colon cast". Sigmoidoscopy showed a congested and erythematous rectum with the remaining portion of the "colon cast" attached to the proximal part of the sigmoid colon. A biopsy from the rectal wall was suggestive of grade IV GVHD. The patient was treated with methylprednisolone, cyclosporin and mycophenolate mofetil, with a partial response (diarrhea and abdominal pain improved), but then he developed multiple other medical complications and died after 3 months.

Acute graft-versus-host disease (GVHD) occurs after allogeneic hematopoietic stem cell transplantation (HSCT) as a consequence of an immune reaction by the donor immune cells against host tissues. About 35% to 50% of HSCT recipients develop acute GVHD.[1,2] Clinically, the diagnosis is suspected when a recipient of HSCT develops any or all of the following signs or symptoms: dermatitis (skin rash), cutaneous blisters, crampy abdominal pain with or without diarrhea, persistent nausea and vomiting, or hepatitis (with elevation of bilirubin and/or liver enzymes).[3] Typically, these symptoms occur before day 100 after the HSCT, but may occur later.[4]

The spontaneous passage of a full-thickness colon cast has been described eight times previously,[5-9] including one case of a mucosal cast. In five cases the etiology was occlusion of the mesenteric artery. In the remaining three cases, one patient had pancreatitis, the other had undergone resection of a lower rectal carcinoma with a sigmoid pouch–anal anastomosis and ileostomy, and the last had undergone Hartmann's procedure sacrificing the inferior mesenteric artery for a perforated diverticulum and pelvic abscess.[5-9] To our knowledge, there are no reports of spontaneous passage of a colon cast in the context of acute GVHD.

CASE

A 23-year-old male underwent allogeneic HSCT for aplastic anemia 90 days prior to presentation. The patient presented to the emergency department with a history of severe lower abdominal pain, bloody diarrhea and fever of 3-days duration. He was discharged from the hospital a few days prior to this presentation after recovering from multiple medical problems following HSCT including *E coli* and *Streptococcus viridans septicemia*, febrile neutropenia, cytomegalovirus (CMV) antigenemia, GVHD involving the skin, and aspergillosis of the lung. On admission the patient was febrile and appeared pale. The skin was hyperpigmented from GVHD. The oral cavity showed features of mucositis. The lower abdomen was tender on palpation. The cardiovascular, respiratory and nervous system examination was unremarkable. Broad-spectrum antibiotics and other supportive measures were begun and the patient was moved to the intensive care unit. On the fourth day of admission the patient passed a 27-cm long, tubular,

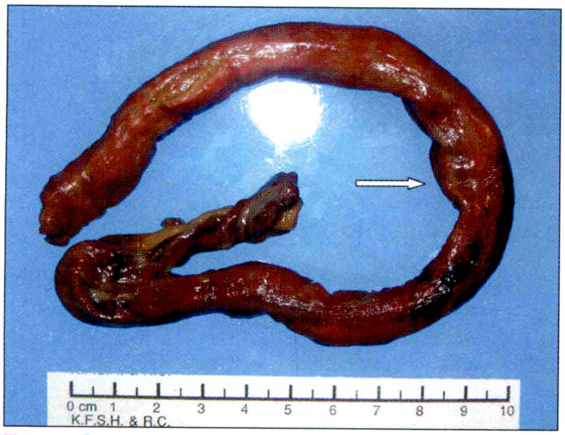

Figure 1. Gross appearance of the colon cast passed per rectum.

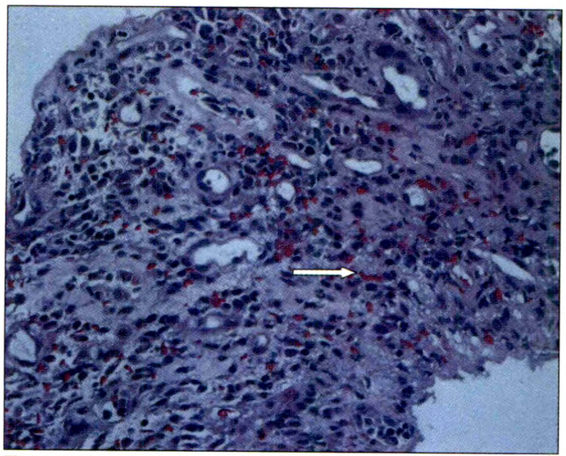

Figure 2. Histology of the sigmoid colon showing granulation tissue and base ulcers suggesting severe graft versus host disease.

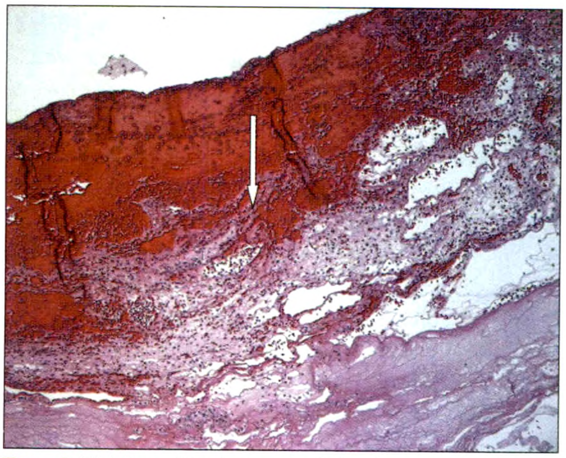

Figure 3. Histology of the "colon cast" showing necrotic fibrinopurulent exudate with bacterial overgrowth.

pinkish-colored fleshy material rectally (Figure 1). This structure was recognized as a "colon cast" and was sent to pathology for histology. The stool examination for culture and sensitivity of *Clostridium difficle* was negative. A CT scan of the abdomen showed non-specific thickening of the large and small bowel including rectum as well as inflammation of the surrounding of the mesenteric fat. A sigmoidoscope was unable to pass more than 25 cm from the anal verge. The sigmoid and rectal mucosa was congested and erythematous. At 25 cm from the anal verge, the residual part of the "colon cast" was seen attached to the colonic wall.

Laboratory tests on admission were as follows: WBC 7.46×10^9/L (normal, 3.9-11×10^9/L), hemoglobin 104 g/L (normal, 110-160 g/L), platelet count 10×10^9/L (normal, 155-435 10^9/L), urea 5.3 mmol/L (normal, 2.5-7.5 mmol/L), creatinine 88 micromols/L (normal, 46-96 micromols/L), potassium 3.1 mmol/L (normal, 3.5-5 mmol/L), sodium 138 mmol/L (normal, 135-147 mmol/L), carbon dioxide 19 mmol/L (normal, 22-31 mmol/L), albumin 26 g/L (normal, 32-48 g/L), bilirubin 21 µmol/L (normal, 0-21 µmol/L), lactic acid 0.8 mmol/L (normal, 5-2 mmol/L), ALT 30 U/L (normal, 10-45 U/L), and alkaline phosphatase 223 U/L (normal, 30-125U/L). The histology of the sigmoid colon showed granulation tissue and base ulcers suggestive of grade IV acute GVHD (Figure 2). The histology of the colon cast showed necrotic fibrino-purulent exudate with bacterial overgrowth (Figure 3). There was no evidence of CMV infection in the histology of the sigmoid colon and CMV culture was negative.

The patient was treated for acute GVHD with methylprednisolone, cyclosporine and tacrolimus. He was later treated with mycophenolate mofetil and anti-thymocyte globulin as per our hospital protocol. Appropriate antibiotics, hydration and other supportive measures were also given. The patient showed some response to treatment with a reduction in the amount of diarrhea. Unfortunately, the patient developed multiple complications afterwards, including gram-negative sepsis, CMV infection, and aspergillosis of the lung, progressive pancytopenia and graft failure. The patient died in the hospital due to multi-organ failure 3 months after admission.

DISCUSSION

About 35% to 50% of HSCT recipients will develop acute GVHD.[10] Acute GVHD is a clinical diagnosis, but other conditions can mimic or coexist with GVHD, such as drug toxicity and infections. Therefore, a biopsy is recommended to confirm clinical suspicion whenever possible.[11]

The pathophysiology of acute GVHD is a complex process. Patients who undergo bone marrow transplantation receive high-dose chemotherapy before the procedure. High-dose chemoradiotherapy damages the host tissues causing release of inflammatory cytokines such as tumor necrosis factor (TNF)-alpha and interleukin 1, which lead to activation of host antigen-presenting cells. The donor T-cells recognize alloantigens on host antigen-presenting cells and activate the donor T-cells. The activated T-cells then proliferate and differentiate into effector cells and secrete cytokines such as interferon (IFN)-gamma. TNF-alpha and IFN-gamma cause further injury to the gastrointestinal epithelium leading to the tissue damage characteristic of acute GVHD.[12]

The gastrointestinal system is the third most common organ involved in acute GVHD. Gut GVHD may involve any part of the gastrointestinal tract and is frequently the most severely involved organ. It is often difficult to treat gut GVHD. Diarrhea and abdominal cramping are generally the hallmarks of gut involvement. Clinical manifestations of gut GVHD include diarrhea, nausea, vomiting and crampy abdominal pain. There may be a large volume of diarrhea, which is often bloody. Abdominal distention and paralytic ileus may develop.[13] Many of the gastrointestinal symptoms are nonspecific and hence endoscopic biopsy confirmation is often needed.

Upper and lower gastrointestinal endoscopy is a useful modality to diagnose acute GVHD and to differentiate it from other causes of diarrhea. Endoscopic findings of gut GVHD may vary from normal to extensive edema, mucosal sloughing or diffuse bleeding from the gut mucosa. The endoscopy may show prominent lesions in the cecum, ileum, and ascending colon. The mucosa involvement can be seen in the stomach, duodenum, and rectum as well.[13]

Endoscopy is a useful tool to grade the severity of acute GVHD, helping the physician to choose appropriate treatment and to predict prognosis. Endoscopic grading is based on the appearance of colonic mucosa during colonoscopy or sigmoidoscopy. Endoscopically, acute GVHD can be classified as stage 1 to 4. Stage 1 is normal appearing mucosa, stage 2 will show a loss of vascular marking of normal colonic vascular pattern or there will be focal mild erythema. Stage 3 acute GVHD will have colonic mucosal edema, erythema, erosions, and/or bleeding. Stage 4 is characterized by colonic ulceration and bleeding.[14] The biopsy is also highly useful for assessing the severity of acute GVHD. Histological grading of GVHD is also divided into 4 classes. Grade 1 GVHD is characterized by increased crypt apoptosis; grade 2 with apoptosis and crypt abscess; grade 3 with individual crypt necrosis; and grade 4 by total denudation of areas of the mucosa.[15] According to the above classification of assessment of severity of gut GVHD, this patient had stage 4 and grade 4 acute GVHD.

To our knowledge, passage of the colonic cast as a manifestation of acute GVHD has never been reported. Previously, one case was reported in the literature, with passage of esophageal mucosal cast as a complication of chronic GVHD following bone marrow transplantation.[16] We propose that the colon mucus cast in this patient was the result of severe GVHD, leading to a total denudation of the mucosa from the deeper layers of the colonic wall.

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A 74-year-old woman with a 1-month history of itching and skin rash

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Ann Saudi Med 2009; 29(3): 234

A 74-year-old woman presented with a 1-month history of itching followed by a rash. The bullous lesions were large and widespread (including lesions on the arm, legs and torso, covering almost 20% of the body surface) (Figure 1). Many lesions were de-roofed and there was evidence of underlying inflammation and the presence of marginal vesiculation. She was hypothyroid (taking levothyroxine) and hypertensive (taking bendroflumethiazide) and had a history of a cerebrovascular accident for which she was taking aspirin. She had a fracture of the shaft of the left femur 3 weeks prior to presentation. She was pale with hemoglobin of 8.1 g/dL with normal renal and hepatic function.

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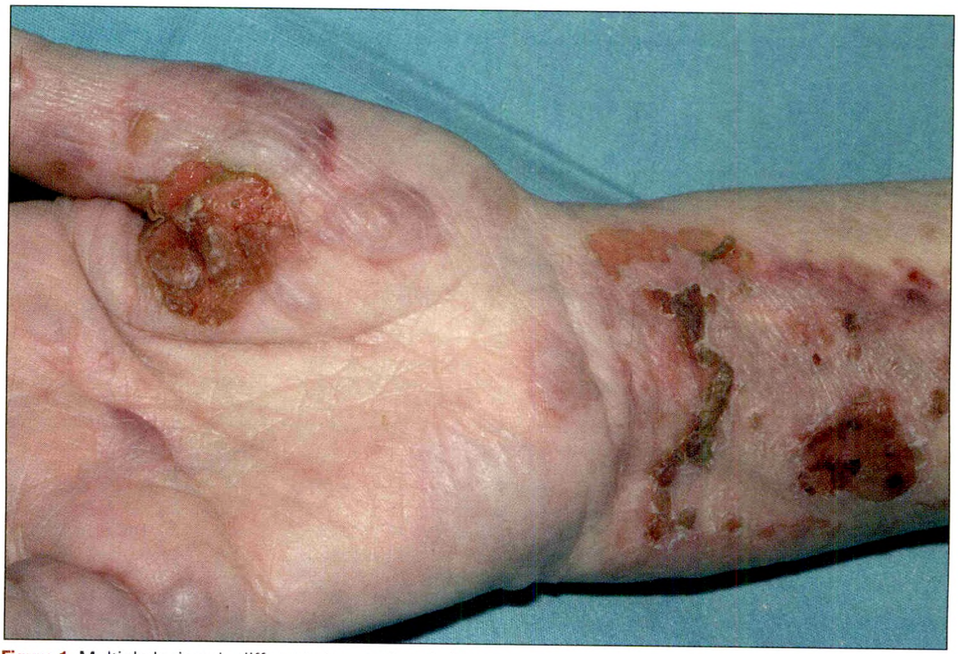

Figure 1. Multiple lesions in different stages of evolution.

Hepatocellular carcinoma in the absence of liver cirrhosis in a treated hepatitis C virus patient

To the Editor: A 65-year-old male patient was referred to King Faisal Hospital and Research Centre after he presented with jaundice, fever, abdominal discomfort and biochemical evidence of chronic hepatitis C virus (HCV) hepatitis with no clinical or histological evidence of cirrhosis. HCV polymerase chain reaction (PCR) was positive and HCV quantitation was 4682 copies/mL. Liver function test (LFT) results were ALT 225 IU/L (reference range, 5-60 IU/L), AST 104 IU/L (reference range, 5-43 IU/L), total bilirubin 20 µml/L (reference range, 5.1-17.0 µmol/L), INR 1.2 (reference range, 0.9-1.1), and albumin 38 g/L (reference range, 35-50 g/L). Liver biopsy showed chronic hepatitis grade II, stage II portal fibrosis and no evidence of cirrhosis. Alpha-fetoprotein was 6 µgm/L. The patient completed a full year of combination therapy of pegulated interferon 3 million units subcutaneously 3 times/week with ribavirin 1000 mg orally daily and achieved a negative viral PCR with normal LFTs. He had 3 years of follow-up with a sustained virological response (sustained loss of detectable virus in response to antiviral therapy) and was then discharged from our clinic and instructed to follow-up at his local hospital. A CT scan at discharge showed no evidence of cancer (image not available). Two years later he was referred back from his local hospital with a huge right hypochondrial mass associated with pain but no jaundice, fever or weight loss. The mass was about 10 cm in diameter, difficult to separate from the liver, ill-defined, lobulated and hard. Basic tests, including CBC and renal profile were normal. ALT 27 IU/L (reference range, 5-60 IU/L), AST 35 IU/L (reference range, 5-43 IU/L), ALP 75 IU/L (reference range, 30-120 IU/L), total bilirubin 14 µml/L (reference range, 5.1-17.0 µmol/L), INR 1.0 (reference range, 0.9-1.1), and albumin 42 g/L (reference range, 35-50 g/L). AFP was 2.3 µgm/L and carcinoembryonic antigen (CEA) was 2.1 µgm/L. Ultrasound of the abdomen showed a huge liver mass (8cm×11cm) and the right portal vein branch was not visualized distally. CT of the abdomen showed the same mass at segment 5 and 8 which was consistent with hepatocelullar carcinoma (HCC) showing the classical triphasic pattern, i.e., heterogenous enhancement in the arterial phase, but early rapid washout in the portal-venous phase leaving the HCC lesion hypo-dense compared to the surrounding normal tissue (Figure 1). The patient underwent surgical removal of both segments (5 and 8). Histopathology of the mass confirmed the diagnosis of HCC. H&E stain showed the HCC pseudoglandular and trabecular pattern (Figure 2) and extensive lymphovasculer invasion. Immunohistochemical stain for CD34 was positive and showed wrapping of the tumor cluster by endothelial cells. The rest of the non-neoplastic livers showed only mild steatosis and no cirrhosis at all (Trichrome stain) (Figure 3).

HCC, which arises from the hepatocytes, is the most common type of primary liver malignancy. It commonly arises in cirrhotic liver. Chronic HCV is a leading cause of cirrhosis worldwide.[1] AFP levels may be normal in more than one third of patients.[2] In our patient, despite having no evidence of cirrhosis and achieving a sustained viral response for 5 years after treatment with combination therapy, he developed HCC. In addition, he had a negative AFP screening test on more than one

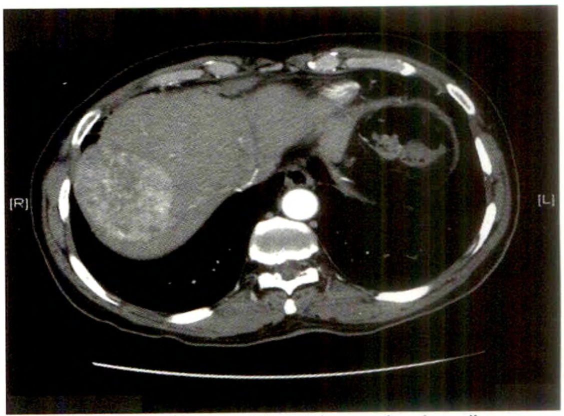

Figure 1. Triphasic CT scan of the abdomen showing a liver mass at segment 5 and 8; a) arterial phase, b) portal-venous phase.

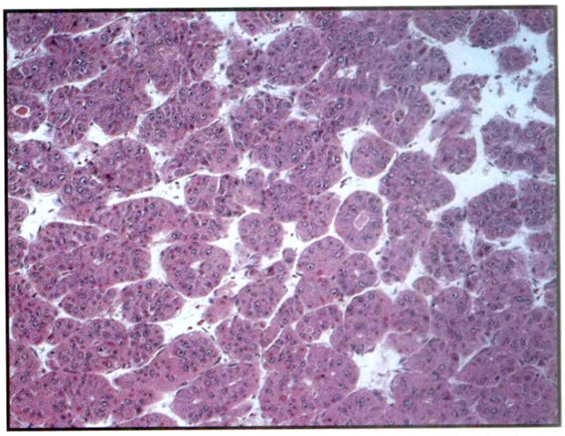

Figure 2. Hepatocellular carcinoma tissue showing classical pseudo-glandular and trabecular pattern (H&E stain).

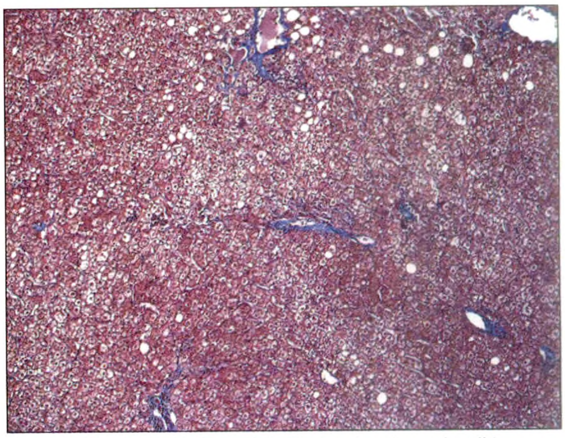

Figure 3. Non-neoplastic hepatic tissue showing only mild steatosis and no evidence of cirrhosis (trichrome stain).

occasion. Okanoue et al[3] conducted a long-term follow-up study of 1246 cases of chronic HCV who received standard pegulated interferon therapy to study the effect of interferon on development of HCC. Interferon lowered the rate of HCC development in both sustained and transient biochemical responders compared to none responders. but did not prevent HCC. In another study by Omata et al[4] that examined the role of interferon treatment on prevention of HCC in chronic HCV patients, development of HCC was strongly associated with stage of liver fibrosis, age and gender. The risk was reduced to 1/5 by interferon, but not prevented among sustained responders compared to untreated patients. Patients at risk of developing HCC should be offered surveillance ultrasound at 3-4 monthly intervals (based on tumor doubling time).[5] A negative initial screening for HCC does not mean that HCC is absent, but only that the tests are insufficiently sensitive. An abnormal screening test requires a triphasic CT or MRI or both, and failure to confirm the diagnosis requires enhanced CT at an interval of 3-4 months.[5]

We found only one case in the literture of HCC in the absence of cirrhosis, but the patient had an additional risk factor, which was porphyria cutanea tarda.[6] An epidemiological study reported HCC with HCV in the absence of cirrhosis in 7 patients, but 5 had coinfection with HBV and the rest had evidence of high alcohol intake (alcohol intake >80 g/day).[7] To our knowldge, our case is the first in a patient with no co-infection and no evidence of other risk factors for HCC apart from HCV infection. Our case suggests that HCC can develop years later in patients with HCV who were treated with interferon-alpha and achieved sustained virological response. It also indicates that normal AFP does not exclude HCC and therefore imaging studies should be used for surveillance for HCC.

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Symptomatic splenoma in a child

To the Editor: Splenoma or splenic hamartoma, described in 1861 by Rokitansky, is a rare benign lesion of the spleen, with only 150 cases having been reported in the literature.[1] They are mostly asymptomatic and are usually discovered incidentally during workup for other unrelated problems or at autopsy. The majority of the reported cases are adult patients; only 20% of cases are in children or adolescents. They have been rarely associated with hematological disorders.[2] We describe splenoma in a 12-year-old female admitted to our department with symptomatic anemia for the past year in the form of easy fatigability, palpitations and exertional breathlessness. Physical examination revealed pallor and a palpable spleen 5 cm below the costal margin. There was no evidence of jaundice, peripheral lymphadenopathy or hepatomegaly. Contrast-enhanced CT of the abdomen revealed splenomegaly and a 5×6-cm minimal enhancing hypodense mass in the lower pole of the spleen (75-80 Hounsfield units) (Figure 1). CT-guided aspiration of the space-occupying mass lesion proved to be inconclusive. A hemogram showed hemoglobin of 6.8 g/dL (normal, 12-16 g/dL); the white blood cell count was 3.7×10^9/L (normal, 3.7-12.9×10^9/L) with a normal differential and platelets of 58×10^9/L (normal, 140-440×10^9/L). Renal, hepatic and coagulation profiles were within normal limits. The reticulocyte count was 4% and the erythrocyte sedimentation rate was 10 mm/hr. The bone marrow showed hyperactivity suggestive of peripheral destruction of blood cellular elements consistent with hypersplenism. The chest x-ray was normal. The tuberculin test and ANA serology were noncontributory.

Pneumococcal and *Haemophilus influenzae* type b (Hib) vaccines were given. The patient underwent elective splenectomy. Intraoperatively, besides splenomegaly, a bulging spherical mass (5×6 cm) having the same consistency as that of the spleen was detected at the lower pole of spleen. There were no perisplenic lymph nodes and the rest of the laparotomy findings were normal. The postoperative course was uneventful, with complete resolution of both clinical and hematological features. The resected spleen measured 16×10×7 cm and weighed 650 g. On sectioning the spleen, a well-circumscribed mass was identified measuring 5×6 cm at its lower pole (Figure 2). The mass was a bulging, spherical, dark red tissue with the same consistency as the surrounding splenic parenchyma. Histologically, the hamartomatous nodule consisted of splenic sinusoidal tissue with no lymphoid follicles (i.e. red pulp) (Figure 3). In addition, there was variable infiltration by chronic inflammatory cells. Futher, on immunoperoxidase staining, the endothelial cells lining the vascular spaces exhibited reactivity for CD8 and factor VIII related antigens and no reactivity to CD34. A diagnosis of a splenoma was made.

Although the diagnosis is established by a histopathological examination, a preoperative diagnosis using a combination of various modern radiological methods may be possible.[3-8] Sonography is a more sensitive modality than CT in demonstrating the lesion, which usually shows hyperechoic masses with cystic components occasionally.[3] Sometimes a hypoechoic splenic mass may be found and color Doppler sonography may reveal blood-flow signals within the mass.[4] Characteristically, CT could reveal splenomegaly and a homogenous or heterogeneous low-density or isodense mass with calcification, or a fatty component. Dense spreading enhancement on dynamic CT and prolonged enhancement on delayed post-contrast scans are noted in a singular mass,[5] but low-density masses may be seen in multiple splenomas after contrast medium administration.[3]

Depending on the histological type (fibrous or non-fibrous), MRI findings in splenomas are distinct. In fibrous splenomas, the MRI scan displays isointensity or hyperintensity on T1-weighted images and hypointensity on T2-weighted images,[4-7] whereas non-fibrous splenomas exhibit isointensity on T1-weighted images and hyperintensity on T2-weighted images.[6,8] The tumors can demonstrate diffuse heterogeneous enhancement on the hepatic artery phase or early dynamic contrast-enhanced scans, which became more uniformly enhanced on delayed images.[5,8] Though splenomas have some distinct radiological features, the final and exact diagnosis depends on histopathological examination. Histologically, the characteristic features are irregular sinus-like vascular channels lined by cells that stain positively with CD8 Factor VIII-related antigen and vimentin.[9] Due to the disordered overgrowth of the red pulp component, splenomas have a variable histological morphology. They should be differentiated from other tumors of the spleen, which include hemangioma, littoral cell angioma, hemangioendothelioma, angiosarcoma and inflammatory pseudotumor. Hemangioma, being the commonest benign tumor of the spleen, is CD8 negative in contrast to the CD8-positive endothelial cells of splenoma. The endothelial cells of littoral cell angioma are CD68 positive and CD8 negative in contrast to splenoma, which is CD68 negative and CD8 positive.[9]

With the use of modern imaging techniques, splenomas may be diagnosed preoperatively, thereby

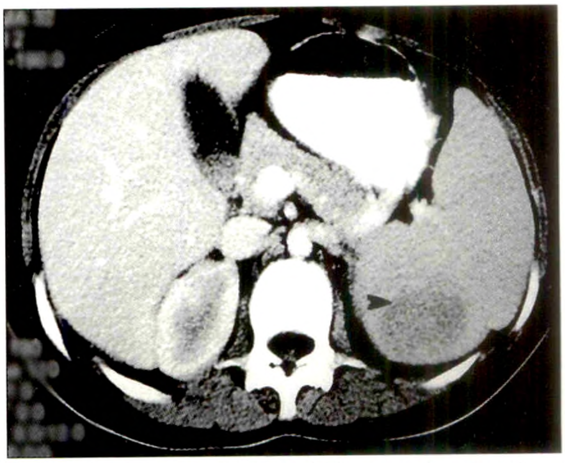

Figure 1. Contrast-enhanced abdominal computed tomography scan demonstrating a low density mass in the lower pole of the spleen (arrow).

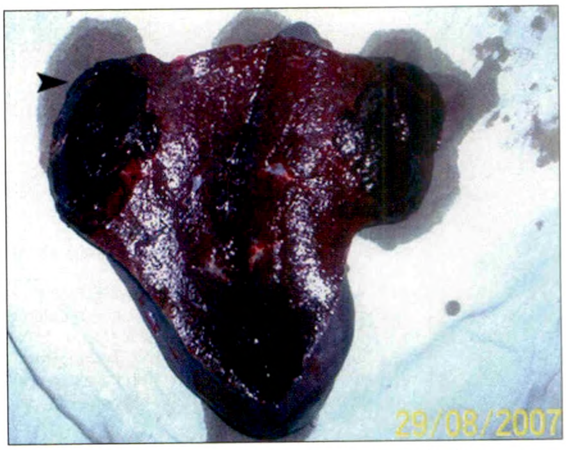

Figure 2. Photograph of the cut section of a resected spleen showing a circumscribed 5×6 cm unencapsulated splenoma (arrow).

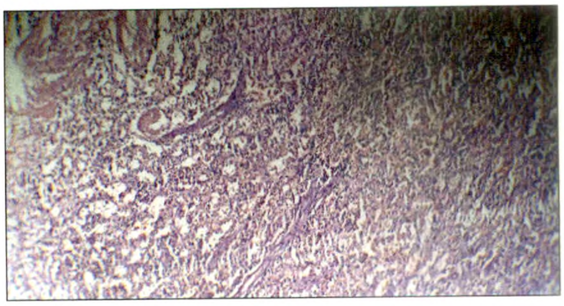

Figure 3. Microscopic image of the splenoma, showing irregularly arranged dilated sinusoids admixed with intervening pulp cord-like elements.

avoiding a splenectomy. While total splenectomy may be necessary if the diagnosis is uncertain or if there is a marked degree of cytopenia or splenomegaly, a partial splenectomy may suffice in some cases.[10]

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Restless leg syndrome in a patient with celiac disease: a coincidence or an association?

To the Editor: A myriad of extraintestinal manifestations of celiac disease have been described,[1] but none have included restless leg syndrome (RLS). We report a case of celiac disease presenting with RLS. A 45-year-old woman was seen in June 2007 for exacerbation of sleep discomfort related to an uncomfortable sensation in the limbs at night that also resulted in daytime somnolence. The sensation decreased with movement and disappeared with walking. She also reported abdominal pain and diarrhea. Repeated colonoscopies in 2002 and 2006 were normal. Her medical history revealed a long-standing anemia refractory to oral iron supplementation and weight loss. A neurological exam was normal. Initial laboratory studies showed a hemoglobin of 9.8 g/dL (reference range, 13-15 g/dL) with a mean corpuscular volume of 82 fL, a mean corpuscular hemoglobin of 26.5 pg/cell (reference range, 3033 pg/cell) serum iron of 11.3 µmol/L (normal range, 8.8-32.4 µmol/L) and serum ferritin of 6.2 ng/mL (normal range, 30-400 ng/mL). Thyroid stimulating hormone, folic acid and vitamin B12 levels were normal. Her 25-hydroxyvitamin D was 7.2 ng/mL (normal, >20 ng/mL). Bone mass densitometry revealed osteoporosis at the spinal level (T score, −3.2). IgA endomysial antibodies and IgA tissue transglutaminase antibodies (>200 RU/mL, normal <20 RU/mL), and IgA antigliadin antibodies (30 UI/mL, normal <5 UI/mL) were positive. Upper gastrointestinal endoscopy revealed an atrophic duodenal mucosa. Duodenal biopsy showed severe villous atrophy with mononuclear infiltrate and epithelial cell damage. A diagnosis of celiac disease with secondary RLS was made. A gluten-free diet and intravenous iron supplementation abated the symptoms of RLS in 6 weeks. At the 6-month visit she had gained 8 kilograms and her serum ferritin level was 57 ng/mL. The patient was diagnosed as having secondary RLS and received parenteral iron supplementation for 5 days.

RLS occurs in 3% to 10% of the general population.[1] It can be associated with a variety of underlying medical disorders, especially iron deficiency.[2] Some authors have suggested that serum ferritin levels were inversely related to RLS severity, but even when serum concentration of ferritin were normal, ferritin was frequently reduced in the cerebrospinal fluid.[2] RLS may be the only clinical manifestation of iron deficiency and when serum ferritin concentration is below 50 ng/mL, a cause of iron deficiency should be pursued.[3] Asymptomatic celiac disease was the cause of iron deficiency in 10% of patients referred to a gastroenterologist[4] and in 8.5% of patients with iron deficiency anemia unresponsive to oral iron therapy.[5] Central nervous system manifestations occur in 10% of celiac disease patients.[6] Cerebellar ataxia is the most frequent, but myoclonus, internuclear opthalmoplegia, dementia and multifocal leucoencephalopathy have all been reported.[6] Peripheral neuropathy has also been reported in association with celiac disease. It occurs generally late in the course of the disease and occasionally during exacerbations of steatorrhea.[7] Recent studies suggest that the mechanism is immunological rather than related to vitamin B deficiency.[5]

To our knowledge, RLS has never been reported as a neurological manifestation of celiac disease. The association of these two diseases may be underestimated. Our patient presented with a simultaneous exacerbation of RLS, abdominal pain and diarrhea. Substantial improvement of her symptoms was achieved by iron supplementation and a gluten-free diet. Iron deficiency or an unknown immune mechanism could explain the association of these two diseases.

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Extended-spectrum β-lactamase *Klebsiella pneumoniae* meningitis treated with tigecycline

To the Editor: Multidrug-resistant bacteria are increasing in prevalence, causing sporadic outbreaks of difficult-to-treat infections. *Klebsiella pneumoniae* is a gram-negative pathogen that is known to cause both community and nosocomial infections. Infections caused by *Klebsiella* that express extended-spectrum β-lactamases (ESBLs) pose a serious challenge to clinicians as they are resistant to a broad range of β-lactams, including third-generation cephalosporins, thus complicating therapy and limiting treatment options. Furthermore, patients infected with these strains may have higher mortality rates and may require a longer hospital stay. Patients are generally sicker and have received more antibiotics than patients who are not infected with ESBL-producing strains.[1,2]

We treated a case of ESBL-positive *Klebsiella meningitis* induced by gunshot trauma, with difficult to remove shrapnel. The patient improved with 2 weeks of tigecycline treatment. Earlier we reported a case of multidrug resistant *Acinetobacter* nosocomial meningitis treated successfully with tigecycline.[3]

A 32-year-old male patient not known to have any chronic illnesses, admitted on 31 August 2008 with a history of a gunshot injury to his lumbar area with opened and shredded meninges. The large bowel was also injured; he underwent laparotomy and bowel resection with primary anastomosis with successful outcome. Many pieces of shrapnel could not be surgically removed and were left in the meninges and spinal canal. He presented with fever and leaking infected cerebrospinal fluid (CSF) from an open lumbar wound, and was taking several different antimicrobial agents (ceftriaxone, metronidazole and ciprofloxacin for a week) without good response. He suffered from bilateral lower limb paraplegia and sensory loss below the umbilical level. Several debridement surgeries and meningeal repairs were attempted, but he continued to suffer from an infected CSF leak. Surface swabs grew ESBL-positive *Klebsiella pneumonia* and *Enterococcus fecalis*. Serial CSF sampling from the upper thoracic spine showed repeated growth of *K pneumoniae* with a similar antibiogram, i.e., sensitive to imipenem, ertapenem, levofloxacin, and ciprofloxacin (tigecycline sensitivity was not available either by disk diffusion or Vitek in the specialty hospital laboratory) (Table 1). Blood cultures taken twice one week apart showed no growth. The patient was initially started on ceftriaxone, ciprofloxacine, teichoplanin, and pipracillin/tazobactam at different intervals during his admission, and then on imipenem plus teichoplanin, but the latter was discontinued as soon as ESBL-*Klebsiella* was identified from CSF. The patient had seizures that were not controlled. Six days later imipenem was discontinued and tigecycline 100 mg loading dose and 50 mg every 12 hours was prescribed for a total duration of 14 days. A week later, parenteral ciprofloxacin was added for 3 days for systemic sepsis. In the meantime he was receiving tigecycline. Two days later, the CSF culture was sterile. The patient was continued on tigecycline and showed remarkable clinical improvement. A CSF culture follow up showed progressive improvement (Table 1). He was discharged home afebrile and in relatively good condition. He was well for 2 weeks and then was readmitted with chest pain and shortness of breath, and

Table 1. Results of cerebrospinal fluid sampling.

	8 Aug	16 Sep	20 Sep	25 Sep
Glucose (mg/dL)	11	54	47	55
Protein (mg/dL)	127	62	95	21
White blood cells (per mm^3)	5200	340	550	90
Differential	P95%, L5%	P33%, L63%	P77%, L23%	
Red blood cells (per mm^3)	1152	120	20	60
Culture	ESBL-producing *Klebsiella*	ESBL-producing *Klebsiella*	ESBL-producing *Klebsiella*	No growth

Shading represents dates when patient received tigecycline, which was continued for 2 additional weeks. ESBL: extended-spectrum β-lactamase. P: polymorphonuclear leukocytes, L: lymphocytes.

diagnosed with pulmonary embolism to which he succumbed in 3 days.

Tigecycline is relatively a novel glycylcycline molecule that escapes the classic resistance mechanisms that bacteria harbor against tetracyclines, i.e. drug efflux pumps and protection of ribosomes. Thus, it has expanded antimicrobial coverage and potent in vitro antibacterial activity against a wide range of clinically important gram-positive and gram-negative aerobic bacteria and anaerobes, including *Staphylococcus aureus*, *Enterococcus* species, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Neisseria gonorrhoeae*, most Enterobacteriaceae, and *Bacteroides fragilis*, but it has limited or no activity against *Pseudomonas aeruginosa* and reduced activity against *Proteus mirabilis*. Its licensed indications so far are skin and soft tissue infections and complicated intra-abdominal infections. Studies are currently ongoing for diabetic foot infection, community-acquired pneumonia and nosocomially acquired pneumionia (Wyeth communication). Thus far no controlled studies are available on treating CNS infections with tigecycline in humans.[3-6] This is our second case of multidrug-resistant gram-negative meningitis in which tigecycline was used with a successful outcome.

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Good reporting of trials and observational studies: Related guidelines and initiatives

EQUATOR

EQUATOR **<http://www.equator-network.org>** (Enhancing the QUAlity of Trials and Other Research) The EQUATOR Network is a new initiative that seeks to improve the quality of scientific publications by promoting transparent and accurate reporting of health research.

STROBE

STROBE **(STrengthening the Reporting of OBservational studies in Epidemiology)** is an international, collaborative initiative of epidemiologists, methodologists, statisticians, researchers and editors involved in the conduct and dissemination of observational studies.

CONSORT (Consolidated Standards of Reporting Trials), is part of a broader push to produce reporting guidelines (RGs) for many different types of research. The main product of CONSORT is the CONSORT Statement, which is an evidence-based, minimum set of recommendations for reporting RCTs. It offers a standard way for authors to prepare reports of trial findings, facilitating their complete and transparent reporting, and aiding their critical appraisal and interpretation. The CONSORT Statement comprises a 22-item checklist and a flow diagram, along with some brief descriptive text.

ASSERT

The ASSERT **(A Standard for the Scientific and Ethical Review of Trials)** initiative is a proposed standard for the review and monitoring of randomized clinical trials by research ethics committees. Among other items, its checklist incorporates certain elements of CONSORT, to ensure fulfillment of the requirements for scientific validity in the ethical conduct of clinical research.

MOOSE

The MOOSE **(Meta-analysis of Observational Studies in Epidemiology)** paper reports the outcome of a 1997 workshop to examine the reporting of meta-analyses of observational studies. It makes recommendations to aid authors, editors, reviewers and readers of observational research.

QUOROM

The QUOROM **(Quality Of Reporting Of Meta-analyses)** conference resulted in the creation of the QUOROM Statement, which consists of a checklist and flow diagram.

STARD

The STARD **(Standards for Reporting of Diagnostic Accuracy)** initiative aims to improve the accuracy and completeness of reporting of studies of diagnostic accuracy in order to allow readers to assess the potential for bias in a study and to evaluate the generalisability of its results.

King Faisal Specialist Hospital & Research Centre

Symposium:

The Health Consequences od Global Warming
06-07 October 2009
17-18 Shawwal 1430

Workshops:

The Future of Healthcare for Adolescents in Saudi Arabia Seminar
03-05 November 2009
15-17 Dhu Al Qada 1430

Courses:

7th Pediatric Intensive Review Course
26 September-01 October 2009
07-12 Shawwal 1430

Academic & Training Affairs
King Faisal Specialist Hospital
& Research Centre
P.O. Box 3354, Riyadh 11211
Saudi Arabia
T: +966-1-442 7238,
F: +966-1-442 4153/442-7237
web_symposia@kfshrc.edu.sa

World Health Organization
Regional Office for the Eastern
Mediterranean

Directory of Health, Medical Conferences and Professional Meetings in the Region

http://www.emro.who.int/conf/

Objectives

To develop and maintain a directory of conferences and meetings organized by government institutions, academic bodies and other non-profit professional organizations in the Region.

The directory will:
- Serve as a vehicle to distribute information on these events to health care professionals and academicians;
- Enhance networking and collaboration between institutions;
- Record professional events for the future reference and archiving of conference proceedings as much as possible;
- Alert health care professionals and academicians to the new conferences related to their speciality.

Section of Colorectal Surgery Fellowship Training Program

A two-year clinical fellowship program that aims to provide the candidate with the basic science, clinical and operative skills to manage patients with colorectal diseases competently. The operative load of the Section is 300 operations annually. The majority of such operations are complex colorectal conditions such as colorectal cancer, fecal incontinence, complex anal fistulae and complicated inflammatory bowel disease conditions. The fellowship provides training into diagnostic and therapeutic colonoscopy such as insertion of colonic stents for bowel obstruction. Moreover, training into endoanal and endorectal ultrasound for the assessment of anal sphincters and staging of rectal cancer will be provided, respectively. An important aspect of the program is training into anorectal physiology testing and the interpretation of such complex data. During training, the fellow will be exposed to Enterostomal therapy and all aspects of stoma care. The Section holds an annual colorectal surgery symposium and the fellow is expected to be an active member in this activity, which includes presentation and publication of medical literature in the area of colorectal surgery. Laparoscopic colorectal surgery will be an integral part of training along with standard open surgery. The Section has a well-established curriculum of teaching activities such as morbidity and mortality meetings, radiology rounds and GI clubs. The fellow is expected to participate actively in these educational activities.

For interested applicants, please contact:
Academic & Training Affairs
T: 442-7214/5
ata@kfshrc.edu.sa

The Palliative Medicine Fellowship Program

King Faisal Specialist Hospital & Research Centre, Riyadh
One-Year Fellowship Program

Applicants:
1. Must be Saudi nationals.
2. Must be Saudi Board (or equivalent)
certified in one of the following specialties:
Family Medicine, Internal Medicine, Anesthesiology, General Surgery &
Boards in other specialites may be considered on indiviudal basis.

For information, please contact: Academic & Training Affairs; King Faisal Specialist Hospital & Research Centre; P.O. Box 3354, MBC 36; Riyadh 11211, Kingdom of Saudi Arabia. T: +966-1-464 7272 ext. 31833; F: +966-1-442 7237

Hepatobiliary-Pancreatic Surgery Fellowship Program

KFSH&RC-Riyadh, Saudi Arabia

Hepatobiliary-Pancreatic Surgery Fellowship Program is a compherehensive structured educational program designed to graduate independent surgeons with high standards of skills, broad knowledge and proficient in clinical decisions. The fellow will attain proficiency in endoscopic procedures, be able to interpret radiological investigations exam as well a take care of basic and complex hepatobiliary-pancreatic surgical procedures.

The Department of Liver Transplantation and Hepatobiliary-Pancreatic Surgery at King Faisal Specialist Hospital & Research Center offers:

- Four qualified hepatobiliary and transplant consultant surgeons with good experience in teaching and commitment to provide academic teaching and training.
- A very good facility in interventinal radiology.
- Equipped Operating rooms and intensive care facility.
- Outstanding internet access for library service for research resources as well as outstanding research facility and database available for research users.

The Fellowship Program is for two years and there are two positions available for application. Qualified candidates can direct their query to:

Academic & Training Affairs
KFSH&RC-Riyadh (MBC 36)
P.O. Box 3354, Riyadh 11211, Saudi Arabia
T: +966-1-442-7215/442-7214
F: +966-1-442-7237

International Congress of Pediatric Hepatology, Gastroenterology and Nutrition

In Collaboration with The International Association for the Study of the Liver (IASL)
24-27 October 2009
Sharm El Sheikh, Egypt

It will be a distinguished event for Pediatricians from all over the world to meet and exchange knowledge. We have faculty speakers from the USA, UK, France, Germany and many other countries.

Find the details at *http://www.hepatogastroevent.org/*
Mortada El-Shabrawi ,MD
Professor of Pediatrics, Cairo University.
Postal Address: 3 Nablos Street, off Shehab Street, Mohandesseen, Cairo 12411, Egypt
T: +2012 313 3705
melshabrawi@kasralainy.edu.eg

3rd International Saudi Orthopaedic Association Conference

18-22 January 2010

Department of Orthopaedic Surgery, King Faisal University will be organizing the 3rd International Saudi Orthopaedic Association Conference in Alkhobar from 18th to 22nd of January 2010.

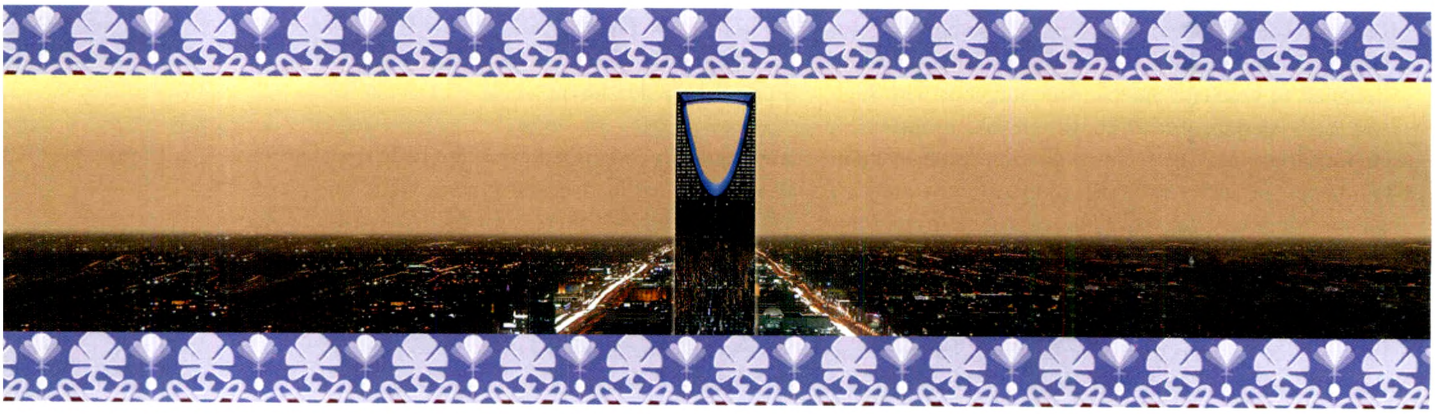
Abstracts can be submitted by e-mail:
SOAC2010@gmail.com or by
Fax: 03-8966735.

Deadline for Abstracts Friday 5th June 2009.

Prof Ibrahim Al-Habdan
Chairman Organizing Committee,
3rd Saudi Orthopaedic Association Meeting
AlKhobar 18-22 January 2010

مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة

CANCER CYTOGENETICS CONFERENCE 2009



2-3 Jumada Al Thani 1430
26-27 May 2009

Prince Salman Auditorium

King Faisal Specialist Hospital and Research Centre
Riyadh, Kingdom of Saudi Arabia

International Speakers

- **Claudia Baldus**, Berlin, Germany
  Charité, University Hospital
- **Georgia Bardi**, Athens, Greece
  Greek General Secretary of Research and Technology
- **Paola Dal Cin**, Boston, USA
  Harvard Medical School
- **Sverre Heim**, Oslo, Norway
  Norwegian Radium Hospital / Rikshospitalet University Hospital
- **Ruben Mesa**, Rochester, USA
  Mayo Clinic
- **Anthony Moorman**, London, UK
  Northern Institute for Cancer Research, Newcastle University
- **Cynthia Morton**, Boston, USA
  Harvard Medical School
- **Daniel Van Dyke**, Rochester, USA
  Mayo Clinic

Organizer

Department of Pathology &
Laboratory Medicine, Section Cytogenetics

Contacts

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Conference Secretary
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Fax +966-1-442-4280
Email garcia@kfshrc.edu.sa

Claudia Walter
Chairperson Organizing Committee
Tel +966-1-442-4228
Fax +966-1-442-4889
Email cwalter@kfshrc.edu.sa

Registration

www.kfshrc.edu.sa/symposia
www. cancer-cytogenetics-2009-kfshrc.com

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FOR HEALTH SPECIALTIES

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OF CONTINUING MEDICAL EDUCATION

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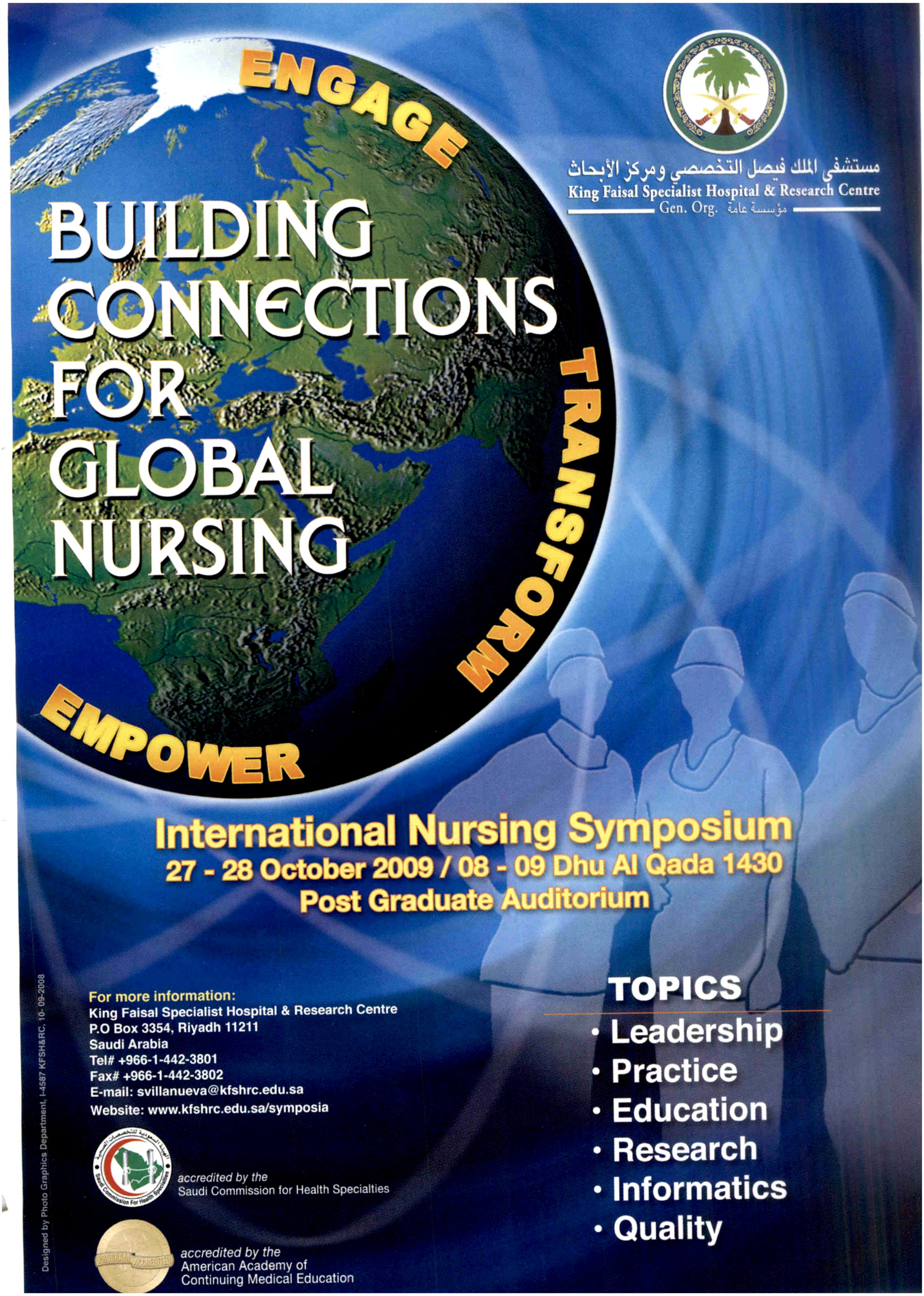

مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة

BUILDING CONNECTIONS FOR GLOBAL NURSING

International Nursing Symposium

27 - 28 October 2009 / 08 - 09 Dhu Al Qada 1430
Post Graduate Auditorium

TOPICS

- Leadership
- Practice
- Education
- Research
- Informatics
- Quality

For more information:
King Faisal Specialist Hospital & Research Centre
P.O Box 3354, Riyadh 11211
Saudi Arabia
Tel# +966-1-442-3801
Fax# +966-1-442-3802
E-mail: svillanueva@kfshrc.edu.sa
Website: www.kfshrc.edu.sa/symposia

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Continuing Medical Education

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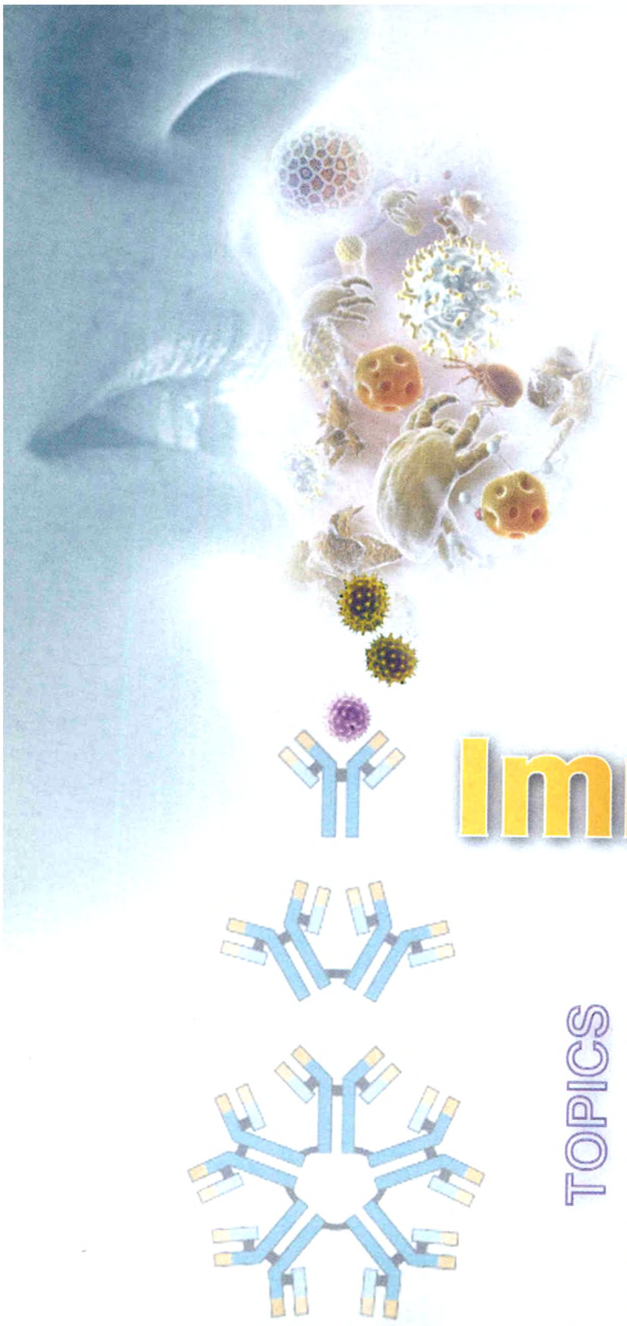

مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة

Allergy Asthma & Clinical Immunology SYMPOSIUM

17-18 November 2009
29-30 Dhu Al Qada 1430

TOPICS

- Asthma
- Epidemiology of allergic diseases
- Allergic Rhinitis
- Role of immunotherapy in allergic diseases
- Food allergy
- Urticaria
- Atopic dermatitis
- Anaphylaxis
- Primary immunodeficiency disorders in Saudi Arabia
- Bone marrow transplantation for primary immunodeficiency disorders
- Advances in management of PID
- Infections of immunocompromised hosts

WHO SHOULD ATTEND

Pediatricians
Internists
General Practitioner
Allergists and Immunologists
Family Practice Physicians
Nurse Practitioner
Pharmacists
Respiratory Care Therapist
Health Care Providers
Other Allied Health Professionals

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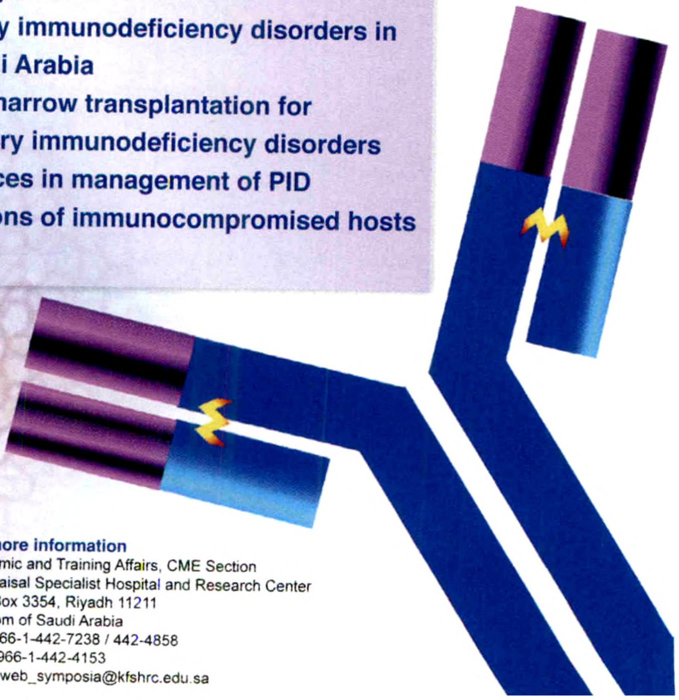

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Email: web_symposia@kfshrc.edu.sa

نسبة الخصر إلى الطول أفضل من منسب كتلة الجسم للتنبؤ بسكري النوع الثاني لدى النساء

مقدمة: أثبتنا مؤخرا أن نسبة الخصر إلى الطول أفضل من منسب كتلة الجسم لغرض التعرف على الرجال الإيرانيين المعرضين لاحتمال الإصابة بسكري النوع الثاني. لذا أجرينا هذه الدراسة لتحديد منسب البدانة الأفضل للتنبؤ بالسكري لدى النساء الإيرانيات.

المرضى والطرق: فحصنا ٢٨٠١ أنثى عمرها ٢٠ عاما فما فوق (المتوسط/الانحراف المعياري للعمر: ١٢,٩/٤٥,٢ سنة) من سكان مدينة إيرانية، ومن غير المصابات بالسكري أو خلل احتمال الغلوكوز وقت المراجعة الأولى. قدرنا القيمة التنبؤية لمعالم البدانة المركزية، وهي محيط الخصر (مخ) ونسبة الخصر إلى الورك (نخو) ونسبة الخصر إلى الطول (نخط) ومنسب كتلة الجسم (مكج)، في التنبؤ بالسكري. قسمنا كل معلم إلى أرباع، وقارنا أدنى ربع بأعلى ربع بعد التعديل للمتغيرات المشوشة، بما فيها العمر وارتفاع ضغط الدم وثلاثيات الغليسريد والكولسترول عالي الكثافة واشتمال تاريخ الأسرة على السكري وخلل احتمال الغلوكوز، باستخدام نموذج متعدد المتغيرات. تم استخدام المنحنيات ROC لتحديد القيمة التنبؤية لكل متغير.

النتائج: خلال فترة متابعة تراوحت بين ١١ شهرا و٦,٣ سنة (الفترة الناصفة ٣,٥ سنة) أصيبت ١١٤ أنثى بالسكري (٤,١٪). كانت نسب الأرجحية للإصابة بالسكري أعلى بدرجة مهمة للأرباع العليا من مكج، ومخ، ونخو، ونخط على التوالي بالمقارنة مع الأرباع الدنيا، ولما شملنا خلل احتمال الغلوكوز في النموذج انخفضت نسب الأرجحية ولكنها بقيت مهمة إحصائيا. بالمقارنة مع مكج كانت نخط ذات مساحة أعلى تحت المنحنى ROC (٠,٧٢ مقابل ٠,٦٩) في حين لم تكن هناك فروق مهمة من حيث المساحة تحت المحنى ROC بين مكج وبين متغيرات القياسات البشرية الأخرى.

الاستنتاج: بالنسبة للنساء الإيرانيات تنبأ مكج، ومخ، ونخو، ونخط بظهور سكري النوع الثاني ولكن نخط كانت أفضل من مكج لهذا الغرض.

المظاهر غير المفصلية لالتهاب المفاصل الرثياني: دراسة الحالات في مستشفى

مقدمة: إن شيوع المظاهر غير المفصلية لالتهاب المفاصل الرثياني (ExRA) يختلف من دولة لأخرى، لذا فقد قمنا بالتقصي عن مدى شيوع ExRA في مستشفى بالمنطقة الغربية بالمملكة العربية السعودية يحوي على عدد محدد من مرضى التهاب المفاصل الرثياني(RA) ، إضافة إلى دراسة المؤشرات المحتملة لتطور ExRA.

المرضى والطرق: أجريت دراسة استعادية على جميع مرضى التهاب المفاصل الرثياني RA في مستشفى جامعي خلال مدة أربع سنوات. تم تصنيف الحالات وفقاً لمعايير التهاب المفاصل الرثياني التابعة لـ American College of Rheumatology لعام ١٩٨٧م ، وتم تسجيل مدى توارد ExRA.

النتائج: من بين ١٤٠ من المرضى الذين انطبق عليهم معيار تشخيص التهاب المفاصل الرثياني RA، أصيب ٩٨ (٧٠٪) بسمات ExRA. ٦١٪ بفقر الدم، ١٠٪ بمشاكل رئوية، وكانت نسب الإصابة بداء كلوي نشواني، والتهاب وعائي، ومتلازمة "فيلتي" ٦٪، ٢٪، ١٪ على التعاقب. كان معدل الوفيات مرتفعاً (١٦٪) لدى المرضى المصابين بالمظاهر غير المفصلية لالتهاب المفاصل الرثياني ExRA. المؤشرات المتسببة بمعدل الوفيات تمثلت في المشاكل الرئوية، الأعمار ما فوق ٥٠ سنة، و الداء الكلوي النشواني.

الاستنتاج: شكلت إصابة المرضى بمظاهر غير مفصلية لالتهاب المفاصل الرثياني ExRA نسبة كبيرة ما أدى إلى عواقب أسوأ للمرض. فقر الدم و مشاكل الجهاز التنفسي كانت الأكثر شيوعاً من بينها. كما أن المعرفة المبكرة والعلاج تعتبر من الأمور الضرورية للتقليل من معدل الوفيات.

السكروز ومصاصة الفم للتخفيف من الألم أثناء إجراء العمليات البسيطة للرضع الخدج: تجربة عشوائية مضبوطة

مقدمة: أظهرت تجارب عشوائية سابقة أجريت لمواليد (حمل كامل المدة) لمعرفة مدى تسكين الألم باستخدام السكروز والغلوكوز والمصاصة، ووجدنا أن استخدام المصاصة يعمل على تخفيف الألم بدرجة أكبر من الغلوكوز والسكروز، لكن لم تختلف نتائج استخدام المصاصة مع السكروز أو بدونه. وقد أجريت الدراسة الأخيرة لتقييم مدى تسكين الألم بالمعايير الدوائية (السكروز، الماء) والمعايير غير الدوائية للرضع الخدج، ولمعرفة ما إذا كان يوجد تآزر بين هذه الطرق في تخفيف الألم أثناء العمليات الجراحية المؤلمة.

المرضى والطرق: أجريت دراسة عشوائية مضبوطة ذات تعمية مزدوجة لـ ٣٦ رضيع خديج (أي حمل لمدة ٣١ أسبوعاً، يتراوح بين ٢٧ و٣٦ أسبوع) تم تقسيمهم عشوائياً إلى ستة أنظمة مختلفة (٠,٥ مللتر مياه معقمة مع مصاصة و٠,٥ مللتر مياه معقمة دون مصاصة و٠,٥ مللتر سكروز بنسبة ٢٤٪ مع مصاصة و٠,٥ مللتر سكروز بنسبة ٢٤٪ دون مصاصة ومصاصة فقط وكمجموعة مضبوطة) أثناء تنويمهم في وحدة العناية المركزة حتى ١٥ يوماً. تم قياس درجات الألم عن طريق سجل الألم لدى الرضع الخدج (PIPP)، مقياس الألم الحاد المثبت.

النتائج: من بين جميع الأنظمة التي تم إتباعها، وجدنا أن أقل درجات الألم ظهرت باستخدام ٢٤٪ من محلول السكروز مع المصاصة. فقد كانت درجة الألم الرئيسية باستخدام السكروز مع المصاصة تبلغ ٠,٧ بالمقارنة مع ١,٤ من المياه المعقمة مع مجموعة المصاصة (درجة الألم < ٠,٥).

الاستنتاج: كان التأثير المشترك بين السكروز والمص غير الغذائي مؤثراً وآمناً من الناحية السريرية لتخفيف الألم أثناء العمليات البسيطة مثل بزل الوريد أو الفحص من عقب القدم لدى الرضع الخدج ورضع الحمل كامل المدة. إلا أننا بحاجة لإجراء المزيد من الأبحاث على هذه الطرق وحدها ومع طرق سلوكية مشتركة أخرى للمواليد.

معدل الولادة القيصرية في المملكة العربية السعودية: مراجعة لعشر سنوات

مقدمة: في ظل الزيادة العالمية في معدل الولادات القيصرية، وما يصاحبها من ارتفاع في معدلات المراضة والوفيات، تم القيام بهذه الدراسة لمراجعة معدلات الولادة القيصرية وبعض العوامل المرتبطة بها خلال فترة عشر سنوات في المملكة العربية السعودية.

الطرق: قمنا باحتساب معدلات الأمومة والتوليد بمستشفيات وزارة الصحة في ١٤ منطقة إدارية وغيرها من المستشفيات الحكومية في تسع (٩) مناطق أخرى، مستخدمين في ذلك دليل الإحصاء السنوي لوزارة الصحة بين عامي ١٩٩٧م و٢٠٠٦م. لم تشتمل الإحصاءات على بيانات من مستشفيات خاصة.

النتائج: ازداد المعدل الإجمالي للولادات القيصرية زيادة يعّتد بها بلغت ٨٠,٢٪، من ١٠,٦٪ في ١٩٩٧م إلى ١٩,١ في ٢٠٠٦م. كانت أعلى نسبة زيادة في المنطقة الشمالية حيث بلغت ٢٦٥٪، بينما كان أقل معدل ٣٢,٨٪ في مستشفيات الهيئة الملكية. أظهرت معدلات الولادة بالجيء المهبلي وبالعمليات الجراحية تدنياً ملحوظاً بلغت نسبته ٣٨٪ و ٢٩٪ على التوالي. كان هنالك ترابط سلبي واضح بين ازدياد معدل الولادات القيصرية وانخفاض الولادات بالجيء المهبلي وبالعمليات الجراحية، علماً بأن حجم الولادات السنوية لم يؤثر في معدل الولادات القيصرية.

الاستنتاج: لوحظ بين عامي ١٩٩٧م و ٢٠٠٦م وجود زيادة ملموسة في معدل الولادات القيصرية بلغت ٨٠٪. هنالك حاجة لوضع استراتيجية وطنية لتقليل هذا المعدل يجب أن تنطوي على تحديث نظام التسجيل الحيوي الحالي. كما نوصي بتوسيع الآليات الحالية لجمع البيانات الوطنية لتشمل بيانات القطاع الخاص ودواعي الولادة القيصرية.

مقاييس ضغط الدم للأطفال والمراهقين السعوديين

مقدمة: قد تختلف مستويات ضغط الدم في الأطفال لأسباب وراثية وعرقية وعوامل اجتماعية واقتصادية. لم تجرى إلى يومنا هذا أي دراسات وطنية كبيرة في المملكة العربية السعودية حول ضغط الدم في الأطفال. ولهذا، سعينا لإنشاء إحصاءات مرجعية نموذجية لضغط الدم للأطفال والمراهقين السعوديين.

المرضى والطرق: قمنا باختيار عينة من الأطفال والمراهقين بواسطة اختيار عينات محتملة متعددة المراحل من الشعب السعودي من سن الولادة إلى ١٨ سنة. وتمثل هذه العينات المختارة الأطفال السعوديين في كل الدولة. وقد تم جمع المعلومات عبر إجراء مسح من منزل إلى منزل لكل الأسر المختارة في ١٣ إقليم في الدولة. تم تحليل المعلومات لدراسة نمط توزيع ضغط الدم الانقباضي والانبساطي وإنشاء قيم مرجعية. تمت مقارنة الشريحة المئوية (٩٠٪) لقيم ضغط الدم الانقباضي والانبساطي لكل عمر مع قيم من دراسات تركية وأمريكية.

النتائج: تمت دراسة إجمالي ١٦,٢٢٦ طفل سعودي من سن الولادة إلى سن ١٨ سنة. هناك ارتفاع في ضغط الدم بشكل ثابت مع تقدم السن في الأولاد والبنات. وقد كان معدل الزيادة السنوية في ضغط الدم الانقباضي (١,٦٦ mm Hg) للأولاد و(١,٤٤ mm Hg) للبنات. أما معدل الزيادة السنوية في ضغط الدم الانبساطي فكان (٠,٨٣ mm Hg) للأولاد و(٠,٧٧ mm Hg) للبنات. وُجد أن مستوى ضغط الدم الانبساطي بشكل حاد في الأولاد بعمر ١٨ سنة. اختلفت قيم الشريحة المئوية (٩٠٪) لضغط الدم الانقباضي والانبساطي في الأطفال السعوديين مقارنة بنظيرتها التركية والأمريكية لكل الفئات العمرية.

الاستنتاج: اختلفت قيم ضغط الدم في هذه الدراسة من تلك القيم الموجودة في الدراسات الأخرى في الدول النامية وفي الولايات المتحدة الأمريكية، مما يشير إلى أن المقارنة عبر الدراسات تعتبر صعبة، وأن على كل الشعوب استخدام مقاييس خاصة بهم لتحديد مستويات ضغط الدم في الأطفال.

الخلاصات العربية

المدونات الطبية السعودية

تصدر المدونات الطبية السعودية مرة كل شهرين عن مستشفى الملك فيصل التخصصي ومركز الأبحاث ، ص.ب ٣٣٥٤ ، الرياض ١١٢١١، المملكة العربية السعودية. يتم توزيع المدونات وإعداد الملخصات العربية بالتعاون مع د. زهير القاوي بواسطة موظفي إدارة الخدمات الإدارية بمستشفى الملك فيصل التخصّصي ومركز الأبحاث.

جميع المراسلات والاستفسارات وطلبات الاشتراك ترسل إلى المحرر الأولَ مكتب المطبوعات (ر.إ ٣٦).

سعر الاشتراك ١٠٠ ريال في السنة للأفراد داخل المملكة و٢٠٠ ريال في السنة للأفراد خارج المملكة و٥٠٠ ريال في السنة للمؤسسات. يمكن فتح اشتراك مجاني للأفراد و المؤسسات في الدول النامية.

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مكتب التحرير:
المدونات الطبية السعودية ر.إ (٣٦)
مستشفى الملك فيصل التخصّصي ومركز الأبحاث ،
ص.ب ٣٣٥٤
الرياض ١١٢١١
المملكة العربية السعودية
هاتف: ٩٦٦-١-٤٦٤٧٢٧٢ تحويلة ٣١٨١٩/٣١٨١٥
فاكس: ٩٦٦-١-٤٦٤٧٢٧٢ تحويلة ٣١٨٧٥
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الرقم التسلسلي القياسي الدولي: ٠٢٥٦ - ٤٩٤٧
١٤٢٧-٠٤

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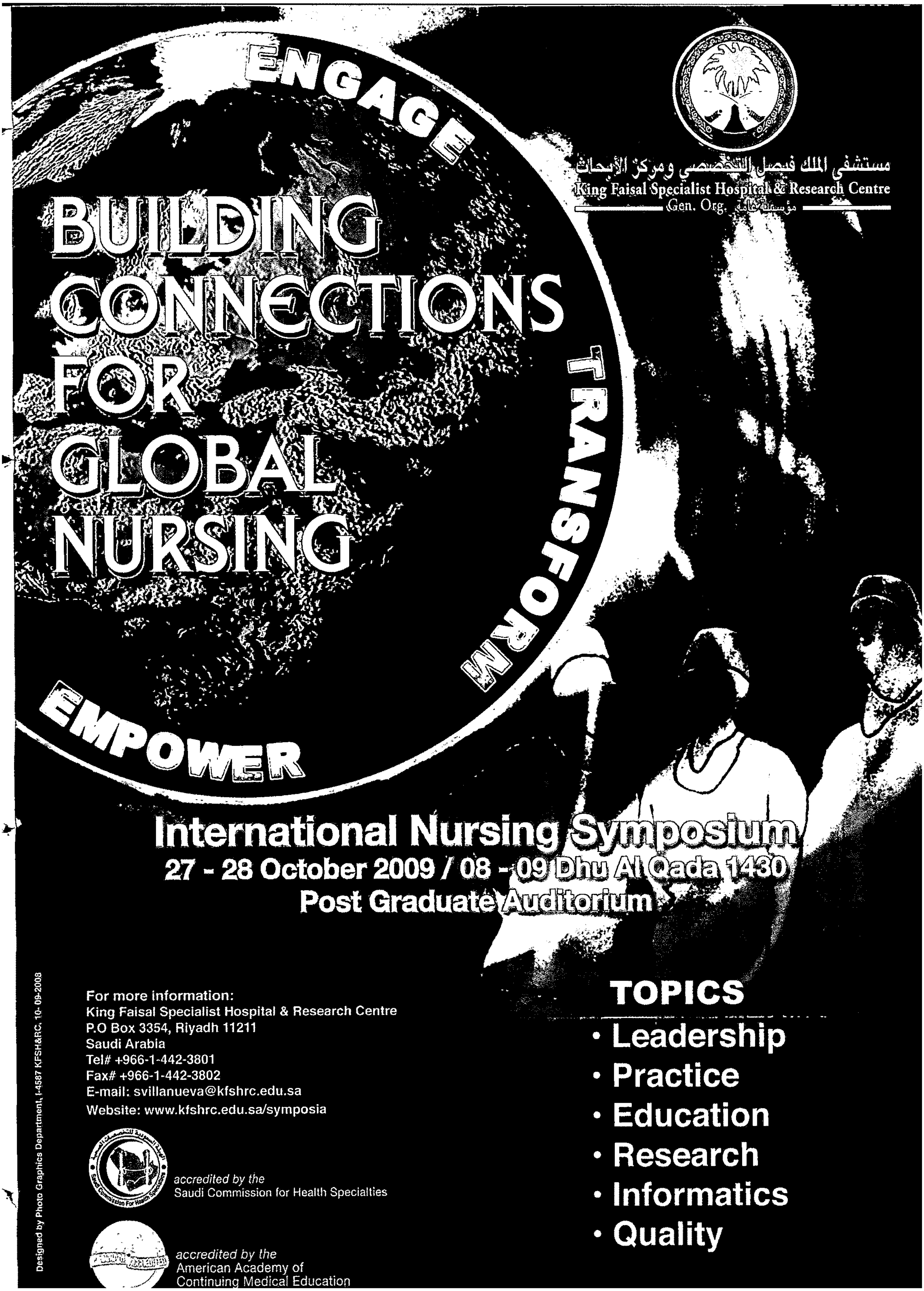

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SUMMARIES

INFECTIOUS DISEASE

Prevalence and molecular characterization of extended spectrum-β-lactamase-producing *Klebsiella pneumoniae* in Saudi Arabia

In 400 *K pneumoniae* isolates from two hospitals in Riyadh, Al-Agamy and colleagues found an ESBL rate of 55%. SHV, TEM and CTX-M β-lactamase genes were found in 97.3%, 84.1% and 34.1% of isolates, respectively. The study confirms the high rate of ESBL-producing *K pneumoniae* in Saudi Arabia in general and the continuing worldwide spread of the $\mathit{bla}_{\text{CTM-X}}$ gene in particular.

FAMILY MEDICINE

Anthropometry and body composition of school children in Bahrain

In a cross-sectional survey of a random sample of 2594 students, Gharib and Rasheed measured height, weight, mid-arm circumference, skin fold thickness, body mass index, and arm muscle area in boys and girls aged 6 to 18 years. When compared with WHO reference standards, the results suggest an increased trend toward adiposity, especially in girls. The authors emphasize the need for intervention programs.

ONCOLOGY AND RADIOLOGY

Accuracy of the Fisher scoring system and the Breast Imaging Reporting and Data System in identification of malignant breast lesions

In a prospective study, Al-Khawari and colleagues compared the MRM BI-RADS category assigned to lesions using the Fisher scoring system to the final diagnosis obtained by tissue sampling and follow-up imaging for 63 breast lesions in 41 patients. Of 55 biopsied, 25 were malignant and 30 were benign. The MRM BI-RADS lexicon using the Fisher scoring system had a high predictive value, especially for malignant breast lesions, and was easy to apply.

ENDOCRINOLOGY

Factors associated with sexual dysfunction in Jordanian women and their sexual attitude

Abu Ali and colleagues interviewed a random sample of 613 married females who attended the National Center for Diabetes, Endocrinology and Genetics in Amman, to find factors associated with female sexual dysfunction and to explore sexual attitudes. Older age and obesity were associated with sexual dysfunction. Further research is needed into the social aspects of female sexual dysfunction.

MENTAL HEALTH

Psychopathology of Saudi secondary school girls in Abha, Saudi Arabia

In a cross-sectional study conducted in ten secondary schools for girls, Al Gelban used a mental health questionnaire to study the prevalence of psychological symptoms and disorders in a random sample of 545 girls. The most prevalent mental symptoms were phobic anxiety (16.4%), psychoticism (14.8%), anxiety (14.3%) and somatization (14.2%). The most prevalent disorders were depression (13.9%), paranoid ideation (13.8%) and interpersonal sensitivity (13.8%). No significant relationship was found with sociodemographic variables. More research is needed to explore the magnitude of the mental health symptoms and disorders in secondary school girls at the national level.

ONCOLOGY

Clinicopathological study of male breast carcinoma: 24 years of experience

Shah and colleagues identified 24 cases of male breast cancer over 24 years at the Sher-i-Kashmir Institute of Medical Sciences in Srinigar. Twenty cases (62.5%) had various risk factors, including testicular abnormalities, infertility, and obesity. Invasive ductal carcinoma was seen in 30 cases (93.7%). Thirty-percent overexpressed HER2 and 30% overexpressed the p53 gene. The *BRCA2* mutation was found in 40% of cases. The 4.1% incidence of the disease indicates that male breast cancer is not as uncommon as presumed in this part of the world.

original article

Prevalence and molecular characterization of extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* in Riyadh, Saudi Arabia

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Accepted for publication May 2009

Ann Saudi Med 2009; 29(4): 253-257

BACKGROUND AND OBJECTIVES: Reports on extended-spectrum β-lactamases (ESBL) production by Enterobacteriaceae, and especially in *Klebsiella pneumoniae*, are few in Saudi Arabia. Therefore, we determined the prevalence of ESBL in *K pneumoniae* from Riyadh and characterized the predominant β-lactamase gene in these isolates.

METHODS: A total of 400 *K pneumoniae* samples were isolated from two hospitals in Riyadh during 2007 and screened for production of ESBL using ESBL-E-strips and combined disk methods. PCR assay was used to detect bla_{TEM}, bla_{SHV}, and $bla_{CTX\text{-}M}$ genes.

RESULTS: Phenotypic characterization identified a high ESBL rate of 55% of *K pneumoniae* isolates. ESBL-producing *K pneumoniae* were PCR positive for SHV, TEM and CTX-M β-lactamase genes with prevalences 97.3%, 84.1% and 34.1%, respectively. Within the CTX-M family, two groups of enzymes, CTX-M-1 and CTX-M-9-like genes were found with prevalences of 60% and 40%, respectively.

CONCLUSIONS: This study confirms the high rate of ESBL in *K pneumoniae* clinical isolates in hospitals in Riyadh. This study demonstrates the worldwide spread of $bla_{CTX\text{-}M}$ genes. This first report of the presence of the $bla_{CTX\text{-}M}$ gene in clincial isolates in Saudi Arabia is evidence of the continuing worldwide spread of this gene.

Extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* have spread rapidly worldwide and pose a serious threat in healthcare-associated infections.[1] ESBLs have spread threateningly in many regions of the world and now comprise over 300 variants (*http://www.lahey.org/studies*). A typical characteristic of ESBLs is their ability to hydrolyze oxyimino-cephalosporins and aztreonam while being inhibited by β-lactamase inhibitors.[2,3] ESBLs arise by point mutations in genes for common plasmid-mediated β-lactamases TEM-1/-2 and SHV-1.[2] The first ESBL SHV-2, which is a derivative of SHV-1, was reported from *ozaenae* in 1983.[4] Several TEM-1 derivatives, however, confer ESBL properties and are prevalent in North America.[3] In recent years, non-TEM and non-SHV plasmid-mediated ESBLs have been reported, mainly the CTX-M enzymes. The CTX-M family, first described in the early 1990s, is the most dominant ESBL among Enterobacteriaceae and is recognized as a rapidly growing family of ESBLs.[5,6] The CTX-M enzymes are the predominant type of ESBL found in many regions of the world, including Asia, South America, Europe and Africa.[7-11] The CTX-M enzymes form a rapidly growing family of currently over 69 enzymes (*http://www.lahey.org/studies*) categorized in five different groups called CTX-M-1, CTX-M-2, CTX-M-8, CTX-M-9 and CTX-M-25.[7]

In Saudi Arabia, few studies have been undertaken to determine the prevalence of ESBL-producing *K pneumoniae*[12-14] However, β-lactamases were not molecularly characterized in these studies. Therefore, this study was devoted to determining the prevalence of ESBL in *K pneumoniae* and the molecular characterization of ESBLs in *K pneumoniae* isolates from Riyadh.

METHODS

Four hundred *K pneumoniae* non-duplicate isolates were collected from hospitalized patients at two different hospitals in Riyadh, Saudi Arabia, during 2007. Susceptibility testing was performed by the disc diffusion method according to Clinical and Laboratory Standards Institute recommendations.[15] The minimum inhibitory concentration (MIC) was determined by an E-strip test (AB BIODISK, Solana, Sweden) as described by the manufacturer. A laboratory control strain, *Escherichia coli* ATCC 25922, was used in the sensitivity test and in the MIC determination. Phenotypic detection of ESBL was carried out by two different methods: 1) the combined disc method using discs containing cefotaxime and ceftazidime with and without clavulanate (Becton Dickinson, USA) with the ESBL phenotype defined as an increase of ≥5 mm in the zone around the disc containing clavulanate compared to the zone of corresponding discs without clavulanate; and 2) using the E-test ESBL-strip (AB BIODISK, Solana, Sweden) with a ceftazidime gradient at one end and a ceftazidime plus clavulanic acid gradient at the other end. These strips were applied according to the procedure described by the manufacturer. ESBL was detected if the ratio of the MIC of ceftazidime to the MIC of ceftazidime plus clavulanic acid was ≥8. PCR methods were used to detect bla_{TEM}, bla_{SHV}, and bla_{CTX-M} using the primers and methods previously described.[9,16,17] A further group-specific CTX-M PCR was performed to differentiate between the CTX-M-1, -2, -8 and -9 groups of enzymes using primers and methods previously described.[18-20] The primers used in this study are listed in Table 1. All PCRs were conducted under standard conditions using plasmid DNA as templates.

Table 1. The primers used in amplification of β-lactamases genes.

Gene	Primers	Nucleotide sequence	Position
TEM	T1	5′-ATT CTT GAA GAC GAA AGG GCC TC-3′	F
	T3	5′-TTG GTC TGA CAG TTA CCA ATG C-3′	B
SHV	NI1	5′-GCC CGG GTT ATT CTT ATT TGT CGC-3′	F
	NI2	5′-TCT TTC CGA TGC CGC CAG TCA-3′	B
CTX-M	CTX-MA	5′-CGCTTTGCGATGTGCAG-′3	F
	CTX-MB	5′-ACCGCGATATCGTTGGT-3′	B
CTX-M-1	ALA2	5′-ATGGTTAAAAAATCACTGCG-3′	F
	P2D	5′-CAGCGCTTTTGCCGTGTAAG-3′	B
CTX-M-2	CTX-M2GF	5′-TTA ATG ACT CAG AGC ATT C-3′	F
	CTX-M2GR	5′- GAT ACC TCG CTC CAT TTA TTG-3′	B
CTX-M-8	CTX-M8GF	5′- TGA ATA CTT CAG CCA CAC G-3′	F
	CTX-M8GR	5′-TAG AAT TAA TAA CCG TCG GT-3′	B
CTX-M-9	C-1	5′-AACACGGATTGACCGTCTTG-3′	F
	C-2	5′-TTACAGCCCTTCGGCGAT-3′	B

F= forward, B=backward

RESULTS

ESBL phenotype was detected in 220 (55%) of 400 isolates. The antibiotic resistance rate and MIC distribution of ESBL-producing *K pneumoniae* are listed in Table 2. The resistance rate to cefotaxime, ceftazidime and amoxicillin/clavulanate were 97% (n=215/220), 95% (n=210/220) and 86% (n=190/220), respectively. A fourth-generation cephalosporin, cefepime, showed moderate activity (47%), but 4.5% (n=10/220) were resistant to cefoxitin and all ESBL-producing isolates were susceptible to imipenem. The resistance to cefoxitin in these isolates may be due to alteration in ompK35 or ompK36 and may not be due to AmpC enzymes because the MIC of β-lactam/β-lactamse inhibitors are markedly reduced in our isolates, but AmpC was not. In addition, the co-existence of other enzymes such as OXA may reduce susceptibility to β-lactam/β-lactamse inhibitors. Among non-β-lactam antibiotics, ESBL-producing isolates showed high resistance to gentamicin and amikacin (88.9% [200/220] and 773.% [170/220], respectively). However, ESBL-producing isolates showed a lower resistance rate of 11% to ciproflaxin.

The PCR assays revealed that the prevalence of SHV, TEM and CTX-M genes was 97.3% (n=214/220), 84.1% (n=185/220), and 34.1% (n=75/220), respectively, in ESBL-producing isolates. Further PCR experiments to characterize CTX-M groups indicated that 45 (60%) of 75 CTX-M-producing isolates carry $bla_{CTX-M-1}$-like genes and 30 (40%) of 75 CTX-M-producers harbor $bla_{CTX-M-9}$-like genes.

DISCUSSION

K pneumoniae is the most frequent ESBL-producing species worldwide. Production of ESBLs was detected in 220 (55%) of 400 clinical isolates of *K pneumoniae* isolated from hospital-acquired infections in Riyadh. There was no difference between the combined disk method and the E-test strip method in the phenotypic detection of ESBL for *K pneumoniae* isolates from Riyadh. Reports on ESBL production by Enterobacteriaceae, and especially in *K pneumoniae*, are few in Saudi Arabia. The overall prevalence of ESBL producers was found to vary greatly in different geographical areas and in different institutes in Saudi Arabia. In our study, the rate of ESBLs-producing isolates collected from two hospitals in Riyadh was relatively high (55%) and was similar to other rates reported from previous studies in Riyadh.[12] However, lower rates for the prevalence of ESBL-producing *K pneumoniae* were detected in Abha and Al-Khobar (27.5% and 12.2%, respectively).[13,21] A higher rate of ESBL production was observed in Riyadh (40% to 55%) followed by Abha (27.5%) and a lower rate was reported in Al-Khobar (12.2%). The variation is difficult to explain, but may be due to differences in the type and volume of consumption of antibiotics and differences in the time of collection of isolates. In Europe, a survey of 1610 *Escherichia coli* and 785 *K pneumoniae* isolates from 31 centers in 10 European countries found that the prevalence of ESBL in these organisms ranged from as low as 1.5% in Germany to as high as 39% to 47% in Russia, Poland, and Turkey.[22] Higher figures of 30% to 60% have been reported for the South American countries of Brazil, Venezuela and Colombia.[23-25] In Asia, ESBL production in Klebsiella has also been reported to be as low as 5% in Japan and ESBL rates in India for *E coli, K pneumoniae and K oxytoca* were 79.0%, 69.4% and 100%, respectively. ESBL-positive *E coli* rates were also relatively high in China (55.0%) and Thailand (50.8%) and Australia with higher rates of 20% to 50% in other parts of the continent.[3,26,27] In Pakistan, the prevalence of ESBL-producing *K pneumoniae* was very high (70%).[28] In the Arabian Peninsula, 23.5% of ESBL-producing *K pneumoniae* were identified as having the ESBL phenotype in Kuwait.[29] However, in the United Arab Emirates, 36% of *K pneumoniae* was found to harbor the ESBL phenotype.[30] In Jordan, 70% of *K pneumoniae* isolates express ESBL phenotypes and this prevalence is alarming.[31]

Resistance to β-lactams, especially third-generation cephalosporins and non-β-lactams, among clinical isolates of gram-negative bacteria is increasing worldwide.[32,33] The overall resistance rate of ESBL-producing *K pneumoniae* isolates studied was alarmingly high to most antibiotics tested including gentamicin, amikacin, cefepime, and trimethoprim/sulfamethoxazole. Imipenem and cefoxitin followed by ciprofloxacin were the antibiotics most active against ESBL-producers. *K pneumoniae* isolates harboring ESBLs are significantly more often resistant to flouroquinolones.[34,35] In the present study only 11.3% of ESBL-producing *K pneumoniae* were resistant to ciprofloxacin. In Iran, resistance to ciprofloxacin was found among 32% of the ESBL-producing *K pneumoniae* strains.[36]

TEM- and SHV-ESBL are derived from parental TEM-1 and SHV-1 by point mutations. TEM-1 and SHV-1 are non-ESBL; however CTX-M enzymes are not derived from non ESBL and consequently all CTX-M enzymes are ESBL. In the present study, the dominant β-lactamase was SHV with a prevalence of 97.3% followed by TEM and CTX-M with prevalences of

Table 2. Minimum inhibitory concentration (MIC) of 220 extended-spectrum β-lactamase-producing *K pneumoniae* isolates.

Antibiotics	Distribution of MIC (µg/mL)																					Resistant	
	≥256	192	128	96	64	48	32	24	16	12	8	6	4	3	2	1.5	1	0.75	0.5	0.38	≤0.25	n	%
Amoxicillin/ clavulanate	40	30	10	35	30	25	30	15	0	5	5	0	0	0	0	0	0	0	0	0	0	190	86.4
Piperacillin/ tazobactam	5	0	0	0	10	0	15	10	11	14	26	14	45	27	43	0	0	0	0	0	0	5	2.4
Cefotaxime	123	7	7	13	10	20	30	4	0	6	0	0	0	0	0	0	0	0	0	0	0	215	97.7
Ceftazidime	175	14	0	6	10	5	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	210	95.5
Aztreonam	160	25	10	5	5	0	10	5	0	0	0	0	0	0	0	0	0	0	0	0	0	215	97.7
Cefepime	35	0	5	0	0	0	5	10	5	5	40	15	20	35	15	30	0	0	0	0	0	105	47.8
Imipenem	0	0	0	0	0	0	0	0	0	0	0	5	25	5	40	15	25	35	40	30	0	0	0
Cefoxitin	1	0	3	1	1	2	1	5	11	0	72	30	23	50	8	7	6	0	0	0	0	10	4.5
Gentamicin	95	10	20	5	5	5	0	10	50	3	7	6	2	1	1	0	0	0	0	0	0	200	88.9
Amikacin	65	10	16	37	42	15	10	1	2	5	5	1	8	6	4	3	0	0	0	0	0	170	77.3
Ciprofloxacin	0	0	2	3	7	0	6	0	0	1	2	2	2	5	9	1	5	15	40	20	100	25	11.4

MIC values in bold are in resistance range.

84.1%, and 34.1%, respectively. In the present study the prevalence of CTX-M enzymes was 34%, but the prevalence of CTX-M enzymes in a study under preparation was 85%. This may be because the present study was done on the isolates were collected during 2007 while in the other study the isolates collected during 2008. In addition to an insertion sequence (*ISEcp1*), which enhances the mobilization of the CTX-M gene, was detected in 60% of CTX-M-producing *Klebsiella* (study under preparation), while the prevalence of *ISEcp1* was relatively low (10%) in isolates included in the present study (Data not included). However, 32 (74%) of the 43 ESBL-producing isolates from Kuwait carried $bla_{CTX\text{-}M}$.[37] In Iran, the prevalence of bla_{SHV} and bla_{TEM} among ESBL-producing *K pneumoniae* was 69.6% and 32.1%, respectively.[36] The prevalence of CTX-M in the present study was lower than the prevalence in Kuwait. However, the prevalence of TEM and SHV was higher than reported in Iran. The higher prevalence of CTX-M in Kuwait is due to most of the CTX-M being detected in non-Kuwaiti immigrants, mainly from South Asia, where CTX-M is endemic.[37] Dissemination of CTX-M ESBL enzymes is worldwide.[7] CTX-M-1 and CTXM-9 groups were detected in our isolates and no CTX-M-2 and CTX-M-8 groups were detected. The occurrence of $bla_{CTX\text{-}M\text{-}1}$-like genes (60%) was higher than $bla_{CTX\text{-}M\text{-}9}$-like genes (40%) in CTX-producing *K pneumoniae* in the present study. In Arab countries, the first description of CTX-M-15 was in Egypt and then in the United Arab Emirates and in Kuwait.[9,37,38] CTX-M-15 is the predominant ESBL in Egypt, United Arab Emirates and in Kuwait.[9,37,38] The present study reporting the CTX-M-15-like gene (CTX-M-1 group) and the CTX-M-14/18-like gene (CTX-M-9 group) is the first report of CTX-M genes in Saudi Arabia.

The bla_{SHV} gene was only found alone in 6.8% (n=15/220) of ESBL-producing isolates with elevated MIC for both cefotaxime and ceftazidime (≥256 mg/L). The presence of SHV β-lactamase alone suggests that these SHV genes are responsible for resistance to extended-spectrum cephalosporins in 6.8% of ESBL-producing *K pneumoniae* isolates. However, the bla_{SHV} gene was found to be associated with the bla_{TEM} gene in 56.8% (n=125/220) with three different patterns of resistance. Seventy-five of 125 (44%) isolates showed a higher MIC for both (≥256 mg/L), while 35 (20%) of 125 isolates exhibited an increase in MIC with cefotaxime and a decrease in MIC with ceftazidime, and 15 of 125 (7.2%) isolates exhibited a decrease in MIC with cefotaxime and an increase in MIC with ceftazidime. From this result either SHV or TEM or both are the ESBLs in 125 of 220 isolates producing ESBL. On the other hand, SHV β-lactamase was present with the CTX-M enzymes in 9.1% (n=20/220) of ESBL-producers. However, the SHV β-lactamase gene was present with both TEM and CTX-M in 25% (55/220). Thirty-five isolates belonged to the CTX-M-1 group with a higher MIC for cefotaxime and ceftazidime, while 20 isolates belonged to the CTX-M-9 group with a decrease in MIC with cefotaxime and an increase in MIC with ceftazidime.

CTX-M enzymes (CTX-M-1 like genes) were co-present with TEM in 5 isolates (2.27%) with an increase in MICs with cefotaxime and ceftazidime (≥256 mg/L). However, the CTX-M family of ESBLs has been increasingly detected worldwide.[5] In the present study, the occurrence of CTX-M-producing *K pneumoniae* was relatively high (34.1%). In India, higher percentages (72%) of ESBL-producers harbor $bla_{CTX\text{-}M}$ genes.[39] In this study, we did not determine which β-lactamase was responsible for resistance to extended-spectrum cephalosporins because these genes were not sequenced. The DNA sequence of these genes must be done to know the type of β-lactamase gene and the prevalence of ESBL genes in ESBL-producing isolates in Saudi Arabia. To our knowledge, there is no published report of the discovery of $bla_{CTX\text{-}M}$ genes in Saudi Arabia.

In conclusion, this study confirms a high rate of ESBLs in *K pneumoniae* in Riyadh, Saudi Arabia, and further demonstrates the worldwide spread of genes coding for CTX-M enzymes in clinical isolates. Most ESBL producers were resistant to oxyimino-cephalosporins and other non-β-lactam agents at high levels.

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original article

Anthropometry and body composition of school children in Bahrain

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Ann Saudi Med 2009; 29(4): 258-269

BACKGROUND AND OBJECTIVES: This study was conducted because of the lack of a comprehensive nationwide assessment of data on the anthropometric status and related health problems in Bahraini school children aged 6 to 18 years.
SUBJECTS AND METHODS: A cross-sectional survey was conducted on the anthropometric status of school children enrolled in the primary, intermediate and secondary government schools in all populated regions of Bahrain. The sample size included 2594 students (1326 girls and 1268 boys) representing 2.5% of the total student population. For sample selection, a multi-stage sampling design was chosen that combined multi-cluster and simple random sampling methods. Anthropometric measurements included height, weight, mid-arm circumference and skin fold thickness at two sites (triceps and subscapular). Anthropometric indices derived were body mass index (BMI) and arm muscle area. The WHO reference standards (2007) and the National Health and Nutrition Examination Survey (NHANES) II data were used for comparison.
RESULTS: Compared to WHO reference standards, the median height of Bahraini children and adolescents in the age range of 6 to 18 years was close to the 25th percentile or lower, while the median BMI during adolescent years was comparable in boys, but higher than WHO standards in girls, reaching the 75th percentile. The cut-off values of BMI for overweight/obesity status (85th and 95th percentile) were higher by 3-6 kg/m^2 compared to WHO standards. While skin fold thicknesses were also higher in Bahraini adolescents compared to their American counterparts (NHANES II), arm muscularity was substantially lower.
CONCLUSIONS: Current study findings for BMI as well as skin fold thicknesses suggest an increased trend toward adiposity among Bahraini adolescents, especially in girls, which puts this age group at a high risk of adult obesity and its consequences. A need for urgent intervention programs is emphasized.

Anthropometry is used to characterize growth patterns and body composition. Growth patterns are indicators of nutritional status of children and are important in developing intervention programs.[1-9] Previous nutritional surveys in Bahrain were limited in their scope and sampling. Some were designed to provide more comprehensive and representative data on the growth patterns of Bahraini children.[1-3] Musaiger et al in 1989 reported that the median heights and weights, triceps skin fold and median arm circumference of boys and girls aged 6.5 to 18.5 years were below the 50th percentiles of the American reference standard (National Center for Health Statistics, NCHS) (3). A decade later (2000), data from the National Growth Survey for Bahraini children showed that the mean body mass index (BMI) of girls aged ≥13 years exceeded that of their American counterparts, but the muscles of children of all ages and both sexes appeared to be underdeveloped. The authors expressed concern over a rising trend for obesity, especially in girls, and emphasized the need for intervention programs.[2] The findings of Al-Sendi et al in 2003 further confirmed the increasing weight gain among the adolescent population.[1] The current research was conducted on a large and representative sample of Bahraini school children and adlolescents aged 6 to 18 years from all the populated regions of the country and formed one of the components of a comprehensive assessment of nutritional status, particularly, anthropometric status (height, weight, body mass index, subscapular skin fold, triceps skinfold thickness, midarm circumference and arm muscle area).

SUBJECTS AND METHODS

The study was cross-sectional and descriptive. Data collection was from January 1999 to May 2001. The target population was Bahraini boys and girls in primary, intermediate and secondary levels in public schools of the 11 populated regions of Bahrain. Information on children aged ≥10 years old was obtained through a self-administered questionnaire while that for younger children was completed by the parents. The age of the children was verified from school records and recorded in whole years.

Sampling

Sample size was determined to ensure a sufficient number of subjects in each age and sex group, according to WHO criteria (1995).[10] An estimated sample size of 2443 was obtained using the standard statistical formula designed to produce valid results for anthropometric variables so that the results are within an approximately 95% confidence interval estimate of the growth parameters. A multi-stage sampling design that combined multi-cluster and simple random sampling methods was chosen to select the sample. Cluster sampling was used in two successive stages: first, for allocation of the schools in each region in proportion to the size of the region and second, for selection of students in proportion to the number of educational levels in each school. Then, the allocated numbers of the students from each level were chosen randomly from different classes.

There were 190 government schools (94 for girls and 96 for boys) in Bahrain during the school year of 1998/1999, enrolling a total of 104189 Bahraini students (52885 girls; 51304 boys) from ages 6 to 18 years.[11] The study included 2594 children (1326 girls, 1268 boys), which represented 2.5% of the total population of school children in Bahrain for the years 1998 to 1999. Parental consent was required for Inclusion of a student in the study. An informed consent form was sent to all the parents of the children. Almost all (99%) parents provided signed consent forms.

Anthropometric measurements

Measurements of height, weight, mid-upper arm circumference (MUAC) and skin fold thickness were obtained for the selected children. All measurements were taken three times and an average value was recorded. Height and weight measurements were taken with the help of a digital electronic scale (SECA Model 930, Hamburg, Germany). The scales were checked for accuracy and calibrated by a specialist prior to the start of fieldwork and during the fieldwork. The technique of recording weight, height and MUAC was done according to guidelines suggested by The WHO Expert Committee (1995).[10] A team of four nurses were trained by one of the investigators (NG) on the correct procedure for taking anthropometric measurements. Their work was supervised periodically during the survey.

Height measurements were taken without shoes. The students were positioned with their feet together and flat on the base plate with their head and back straight against the vertical measuring rods. Once the correct position was achieved the interviewer lowered the head plate until it just touched the top of the student's head, and while maintaining this position, he or she was asked to stand as tall as possible, without lifting the heels. Measurements were made to the nearest 0.1 cm. Weight measurements were taken in light clothing; shoes, trainers, jackets, heavy jewelry, keys and wallets were removed. Weight was recorded to the nearest 0.1 kg.

MUAC was measured with the student's left arm at 90° across the body. Using a conventional non-stretchable tape (metal tape from Chasmors LTD, London), the distance between the inferior border of the acromion and the tip of the olecranon process was measured and the mid-point on the student's arm was marked. The insertion tape was then placed horizontally at the level of the mid-point without compressing the tissues and a circumference measurement was taken to the nearest 0.1 cm.

Triceps skin fold (TSF) and sub-scapular skin fold (SSF) thickness were measured using a Harpenden skin fold caliper (Crymych, Wales, UK). Measurement of TSF was taken on the posterior aspect of the bare extended right arm, over the triceps muscle, midway between the lateral projection of the acromion process of the scapula and the inferior margin of the olecranon process of the ulna. The caliper tips were placed perpendicular to the long axis of the skin fold, and the reading on the dial was taken to the nearest 0.1 mm. SSF was measured 2 cm below the lowest or inferior angle of the scapula. The long axis of the skin fold was at a 45° angle directed to the right side. With the student's arms relaxed to the sides, the skin was grasped 1 cm above and medial to the site along the axis. A measurement was taken to the nearest 0.1 mm. Both measurements were taken according to the methods described by Nieman and Lee.[12]

Anthropometric indices

Body mass index (BMI) was calculated by using the formula weight (kg) divided by height (m)squared.[10] Cross-sectional arm muscle area (AMA) was estimated from upper arm circumference (UAC) and TSF, assuming a circular and concentric model, using the formula[10]

$$\text{AMA (cm) 2} = [\text{UAE} - (\pi\_\text{TSF})]/4\pi$$

For construction of height, weight and BMI percentiles, a statistical analysis was performed using the LMS (lambda, mu, sigma) method. The calculation of the

Table 1. Anthropometric measurements and indices for Bahraini girls.

Age	n	%	Height (cm)	Weight (kg)	Body mass index (kg/m^2)	Subscapular skin fold thickness (mm)	Triceps skin fold thickness (mm)	Midarm circumference (cm)	Arm muscle area (cm)
6	50	4	118.7 (6.4)	21.1 (5.1)	14.8 (2.4)	7.1 (4)	10.5 (4.7)	13.6 (4.8)	10.6 (7.7)
7	87	7	120 (5.7)	21.6 (5.8)	14.9 (3.6)	7.2 (3.3)	10.9 (4.7)	14.4 (5.6)	12.1 (8.9)
8	90	7.3	125.4 (5.7)	24.8 (7.7)	15.5 (4.1)	8.2 (4.5)	13 (7.8)	13.6 (4.9)	9.8 (8.3)
9	119	9.6	130.3 (7.2)	28.1 (8.1)	16.4 (3.8)	9.1 (5.4)	13.7 (7.3)	15.9 (6.3)	13.9 (10.8)
10	116	9.3	136.4 (7.9)	33.9 (10.7)	17.9 (4)	10.7 (6.5)	15.4 (8.3)	16.7 (8.7)	16.8 (27.3)
11	123	9.9	141.8 (7.5)	38.3 (11.5)	18.8 (4.6)	12.3 (7.3)	16.5 (8.9)	18 (7.2)	17.2 (13.3)
12	104	8.4	147.6 (7.3)	43.7 (12)	19.9 (4.8)	12.7 (7.4)	17.8 (8.8)	18.7 (7.7)	18.1 (14.1)
13	83	6.7	152.8 (6.8)	50.9 (12.9)	21.6 (4.5)	15.3 (8.1)	22.1 (9.8)	22.8 (7.4)	23.9 (13.6)
14	97	7.8	156.1 (6.4)	54.3 (14.3)	22.2 (5.3)	16.1 (9.4)	23.4 (10)	22.2 (8.4)	22.6 (15.6)
15	71	5.7	155.5 (5.2)	54.3 (13.2)	22.4 (5)	17.2 (10.4)	23.7 (12)	24.7 (5.5)	25.4 (12)
16	108	8.7	156.6 (5.9)	56.7 (13.2)	23.1 (5.1)	19.4 (9.6)	26.7 (10.4)	25.1 (5.5)	23.9 (12.5)
17	97	7.8	156.3 (6.6)	57.6 (16.8)	23.3 (5.4)	20 (10.4)	28.9 (13)	27.3 (6.4)	28 (13.4)
18	90	7.3	156.6 (6.1)	57.2 (12.6)	23.3 (4.7)	20.2 (10.1)	29.2 (12.6)	26.9 (5.2)	26.1 (11.5)
Total	**1235**	**100**	**143.2 (14.9)**	**42 (17.6)**	**19.6 (5.5)**	**13.6 (9.0)**	**19.5 (11.3)**	**20 (8.2)**	**19.2 (15.4)**

Values are mean (standard deviation).

smoothed percentiles was obtained using standard software.[13]

Reference standards

Height, weight and BMI were compared to the newly recommended NCHS/WHO reference standards (2007);[14] MUAC and AMA were compared to data of the US National Health and Nutrition Examination Survey (NHANES) 2 of 1971-1974, which were derived from population samples of the National Center for Health Statistics (NCHS) growth percentiles for children[15] and TSF and SSF were compared to US data adopted from the NCHS, 1987.[16]

Pilot study

A pilot study was conducted on 60 boys and 60 girls (5% of sample) who were chosen randomly from six schools of one region. Thirty students of each gender were selected from the primary schools and 15 each from the intermediate and secondary schools. Each academic level was represented. The pilot study was done to identify any possible administrative difficulties, the accuracy of the procedures involved, time motion and the response rate of students. No modifications were required in the anthropometric component of the study.

RESULTS

Of 2594 students in the study population, 53.4% (n=1386), 23.0% (n=596) and 23.6% (n=612) were from primary, intermediate and secondary schools, respectively. Their ages ranged from 6 to 18 years, with a mean (SD) age of 12 (3.6) years. Almost 54% (n=713) of the girls (12 to 18 years) and 48% (n=606)of the boys (13 to 18 years) were in the adolescent age group as per criteria defined by Story et al.[17]

Tables 1 and 2 show the means for the anthropometric variables by age and gender. The means of the anthropometric measurements gradually increased with age in both genders with the mean height of the girls and boys beyond the ages of 16 years and 17 years, respectively, remaining relatively unchanged. The mean MUAC and AMA for girls gradually increased with age up to 17 years, but showed a slight decrease thereafter. A similar trend by age was observed in boys for body weight, BMI and MUAC.

Figures 1 and 2 show the median heights and BMI of the study subjects plotted on WHO smoothed percentile charts.[14] The median heights of Bahraini boys and girls aged 6 to 7 years were close to the 50th percentile of the WHO standards or higher; thereafter, median heights were closer to the 25th percentile up to age 18 years in boys and 13 years in girls. In late adolescence, the median

Table 2. Anthropometric measurements and indices for Bahraini boys.

Age	n	%	Height (cm)	Weight (kg)	Body mass index (kg/m^2)	Subscapular skin fold thickness (mm)	Triceps skin fold thickness (mm)	Midarm circumference (cm)	Arm muscle area (cm)
6	31	2.6	118 (5.3)	20.2 (4.9)	14.3 (2.6)	5.5 (6.0)	7.2 (5.3)	17 (2.4)	16.9 (2.9)
7	89	7.5	121.5 (5.8)	21.5 (5.0)	14.6 (2.5)	5.3 (3.2)	7.5 (3.2)	17.5 (2.1)	17.7 (3.3)
8	113	9.5	126 (5.8)	23.7 (5.5)	15.2 (2.7)	6 (4.0)	7.6 (4.3)	17.8 (2.5)	19.3 (4.0)
9	98	8.2	130.5 (6.4)	27 (8.8)	15.8 (3.9)	7.1 (6.1)	8.6 (6.6)	19 (3.5)	21.3 (4.7)
10	101	8.5	134.5 (6.7)	29.7 (9.5)	16.5 (4.1)	7 (7.6)	9.7 (5.9)	20 (3.2)	22.2 (4.7)
11	110	9.3	139.5 (6.7)	33.6 (10.4)	16.6 (4.0)	7.1 (7.9)	9.2 (6.7)	20.4 (3.4)	23.5 (5.0)
12	90	7.6	146.3 (9.4)	40.6 (14.5)	18.7 (5.0)	9.8 (11.0)	11.7 (9.4)	22.6 (4.4)	27.5 (7.6)
13	106	8.9	151.3 (8.9)	42 (12.0)	18.9 (4.1)	8.8 (9.1)	11 (7.2)	23.3 (3.3)	28.5 (6.7)
14	98	8.2	162 (9.1)	51.7 (14.7)	19.5 (4.5)	9 (9.6)	10 (8.2)	24.5 (3.9)	35.3 (7.9)
15	85	7.1	164 (8.3)	53.2 (14.2)	19.7 (4.2)	8.3 (10.0)	8.7 (8.9)	24.5 (4.2)	36 (9.4)
16	86	7.2	169 (6.9)	61.7 (16.7)	21 (5.8)	9.4 (10.4)	9.8 (9.6)	27 (4.3)	43.3 (8.4)
17	90	7.6	171 (6.6)	63.2 (21.4)	21.6 (7.6)	11.7 (14.4)	11.1 (10.9)	27.8 (4.9)	47.7 (11.1)
18	76	6.4	171 (6.5)	64.9 (10.8)	21.8 (3.3)	11 (6.2)	8.8 (6.7)	28 (3.4)	47 (10.9)
Total	**1173**	**100**	**145 (18.9)**	**39.9 (20.1)**	**18.2 (5.2)**	**8 (9.2)**	**9 (7.7)**	**22.5 (5.1)**	**26.9 (12.4)**

Values are mean (standard deviation).

Table 3. Distribution of percentiles of height among Bahraini girls and boys aged 6-18 years (2000-2001) compared to WHO growth reference for 2007.[14]

Age (y)	Height Percentiles (cm)									
	Girls					Boys				
	Total	n	5	50	95	Total	n	5	50	95
6	51	50	110.6 (106.7)	118 (115.1)	132.5 (123.5)	36	31	111.9 (107.8)	118 (116)	130.6 (124.1)
7	89	87	110.6 (111.8)	119.5 (120.8)	130.9 (129.8)	100	89	113.8 (113)	121.5 (121.7)	133 (130.4)
8	96	90	114.6 (117)	126 (126.6)	133.2 (136.1)	116	113	115.9 (118)	126 (127.3)	135 (136.6)
9	126	119	119 (122.4)	130 (132.5)	145 (142.5)	100	98	120.5 (122.7)	130.5 (132.6)	142 (142.5)
10	120	116	125 (128.1)	135 (138.6)	151.1 (149.2)	106	101	120.2 (127.3)	134.5 (137.8)	145.9 (148.3)
11	131	123	130 (134.1)	141 (145)	153.5 (155.9)	114	110	130 (132)	139.5 (143.1)	151.7 (154.2)
12	111	104	134.6 (140)	148.3 (151.2)	159 (162.5)	90	90	132.3 (137.4)	146.3 (149.1)	166.5 (160.7)
13	93	83	139.7 (145)	153 (156.4)	162.9 (167.8)	108	106	136 (143.8)	151.3 (156)	165.3 (168.3)
14	105	97	145.9 (148.4)	157 (159.8)	168 (171.2)	113	98	144.5 (150.5)	162 (163.2)	174 (175.8)
15	84	71	147.5 (150.4)	155 (161.7)	163.6 (173)	93	85	146.6 (156.1)	154 (169)	178.4 (181.8)
16	112	108	147 (151.4)	156.5 (162.5)	168 (173.7)	94	86	155.4 (160.1)	169 (172.9)	181.3 (185.7)
17	106	97	147 (151.8)	155 (162.9)	168.6 (173.9)	98	90	160.6 (162.6)	171 (175.2)	180.7 (187.7)
18	96	90	146.6 (152.2)	157 (163.1)	167.5 (173.9)	82	76	160.4 (163.9)	171 (176.1)	182.2 (188.4)
Total	1320	1235				1250	1173			

WHO percentiles are in parentheses.

Table 4. Distribution of percentiles of body mass index among Bahraini girls and boys aged 6-18 years (2000-2001) compared to WHO growth reference for 2007.[14]

Age (y)	BMI Percentiles (kg/m²)											
	Girls						Boys					
	Total	n	5	50	85	95	Total	n	5	50	85	95
6	51	50	12.2 (13.1)	14.2 (15.3)	17.1 (17.1)	20.6 (18.4)	36	31	12.3 (13.4)	14.3 (15.3)	18.1 (16.8)	22 (17.9)
7	89	87	11 (13.1)	14.2 (15.4)	17.4 (17.4)	20.8 (18.8)	100	89	12.4 (13.5)	14.6 (15.5)	17.7 (17.1)	21.2 (18.3)
8	96	90	10.9 (13.3)	14.6 (15.7)	18.5 (17.8)	23.1 (19.4)	116	113	12.1 (13.7)	15.2 (15.7)	17.4 (17.5)	21 (18.8)
9	126	119	12.2 (13.6)	15.7 (16.1)	19.7 (18.4)	23.6 (20.2)	100	98	12.9 (13.9)	15.8 (16)	21.4 (18)	24.6 (19.5)
10	120	116	13.4 (13.9)	16.9 (16.6)	22.2 (19.1)	26.4 (21.1)	106	101	13.2 (14.1)	16.5 (16.4)	21.6 (18.6)	25.8 (20.2)
11	131	123	13.2 (14.4)	17.3 (17.2)	23.8 (20)	29.1 (22.2)	114	110	13.9 (14.5)	16.6 (16.9)	21.3 (19.3)	25.1 (21.1)
12	111	104	14.9 (14.9)	18.3 (18)	25.4 (20.9)	29.4 (23.3)	90	90	14.6 (14.9)	18.7 (17.5)	24.9 (20.1)	33.6 (22.1)
13	93	83	15.9 (15.5)	20.9 (18.8)	25.3 (21.9)	32 (24.4)	108	106	14.8 (15.4)	18.9 (18.2)	22.8 (20.9)	28.6 (23.1)
14	105	97	16.1 (16)	20.7 (19.6)	27.6 (22.9)	30.7 (25.5)	113	98	15.3 (16)	19.5 (19)	24.8 (21.9)	28.6 (24.2)
15	84	71	16.2 (16.5)	21 (20.2)	29.4 (23.7)	31.8 (26.3)	93	85	15.1 (16.5)	19.7 (19.8)	25.6 (22.8)	30.6 (25.2)
16	112	108	17.3 (16.8)	21.8 (20.7)	27.6 (24.2)	34.9 (27)	94	86	16.8 (17.1)	21 (20.5)	27.3 (23.7)	34.2 (26.1)
17	106	97	17.1 (17)	22.4 (21)	27.9 (24.7)	34.4 (27.4)	98	90	16 (17.5)	21.6 (21.1)	31.2 (24.4)	40.2 (26.9)
18	96	90	16.9 (17.1)	22.4 (21.3)	28.9 (24.9)	30.8 (27.7)	82	76	18.1 (17.9)	21.8 (21.7)	25.8 (25)	29.3 (27.5)
Total	1320	1235					1250	1173				

WHO percentiles are in parentheses.

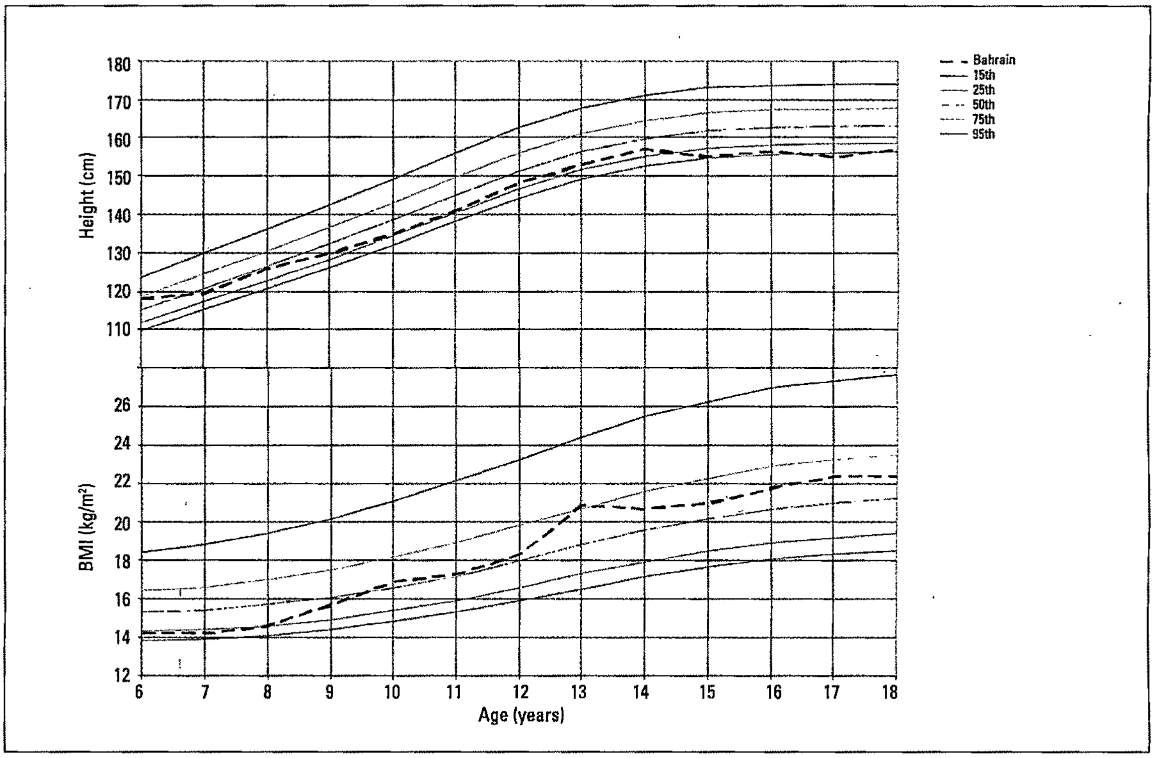

Figure 1. Median heights and BMI by age for girls compared to WHO growth reference for 2007 (15th, 25th, 50th, 95th percentiles).[14]

height of girls showed a decline to the 15th percentile. The median BMI remained close to the WHO 50th percentile at all ages in boys and up to age 12 years in girls. In girls, BMI increased to between the 50th and 75th percentile during adolescence.

The median values of TSF and SSF indicating subcutaneous fat, were generally close to the US 50th percentile during pre-adolescent years in both genders but increased thereafter to lie between the 75th and 85th percentiles (Figures 3 and 4). The median MUAC values plotted on NHANES-II-US[15] smoothed percentiles were close to the 5th percentiles of the US standards for preadolescent girls, but increased thereafter reaching the 50th percentile at the age of 17 years. In boys, the values for MUAC remained close to the 25th percentile of the US standards at all ages (Figure 5). The median AMA of girls fluctuated between the 5th and 25th US percentile while that in boys remained close to the 25th percentile at all ages.

Tables 3 and 4 show that the Bahraini median percentile values for height of boys and girls were in general, lower than those of WHO at the 5th, 50th and 95th percentiles especially during adolescence when values were 3 to 6 cm lower than the reference standards. On the other hand, BMI values for Bahraini adolescents were higher by 3 to 6 kg/m² at the 85th and 95th percentiles compared to WHO values.

DISCUSSION

Anthropometric data are widely used to estimate the nutritional status of children. The height and weight of a child are useful indices of development, reflecting the various influences on growth, including nutrition. Indeed, the monitoring of a child's increase in height and weight by age using growth charts is widely used to identify failure-to-thrive or over nutrition.[10,18]

Among the scant number of published studies on anthropometric characteristics of Bahraini school children, only a few[2,3] have reported data on a wide range of age categories of both genders, such as those in the present study. Moreover, compared to other studies[14-16] the current research provides a much more comprehensive assessment of children's physical growth through the use of a variety of anthropometric indicators. Though the age of 6 years was less well represented than others due to few children of this age enrolled in grade 1 (36.4% girls and 26.5% boys), the number of children ≥7 years old were sufficient in each age group to estimate the standard deviation and percentiles with good precision. In general, the current study population could be considered representative of Bahraini school children.

Current data shows that Bahraini children are

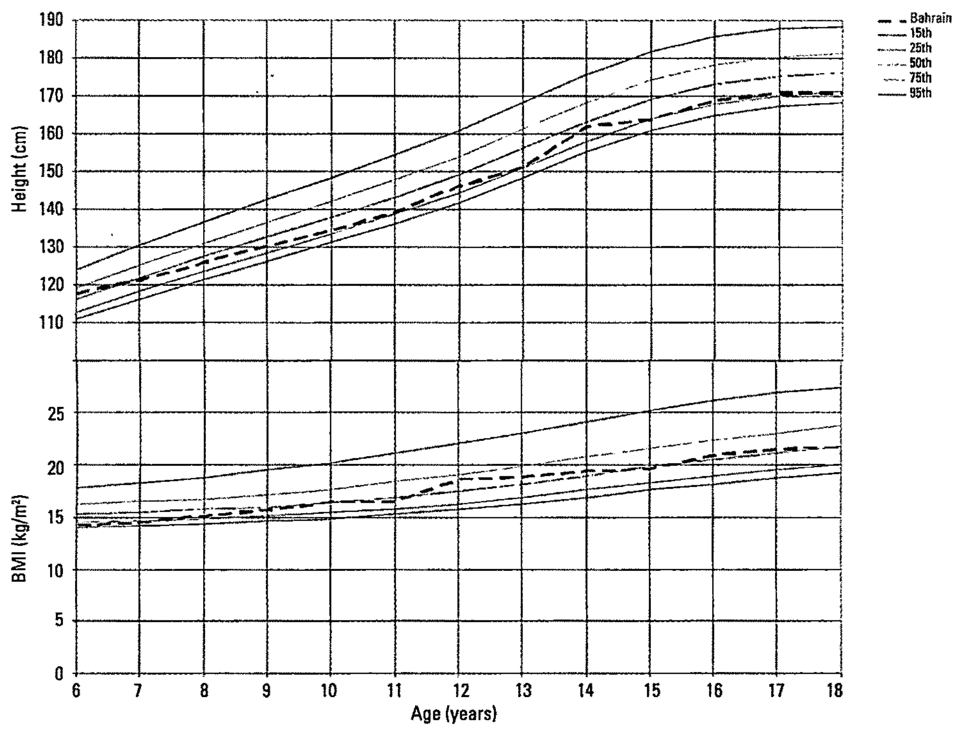

Figure 2. Median heights and BMI by age for boys compared to WHO growth reference for 2007 (15th, 25th, 50th, 75th, 95th percentiles).[14]

shorter at all ages compared to their NCHS/WHO reference counterparts except for the age group of 6 to 7 years old. This suggests that children had a good growth phase during the preschool age period and excludes the probability of severe or prolonged malnutrition in the critical growth periods of intrauterine life, infancy and the preschool ages. Similar results were reported by Rasheed et al[6] in their study on Saudi children.

Compared to findings of an earlier study,[3] the growth performance of Bahraini children has changed. Median heights of Bahraini children two decades ago fell between the 5th and 25th percentiles of the NCHS/ US standards, while median weights were below the 50th percentiles of the standard. Current findings suggest that Bahraini children are heavier and slightly taller than their counterparts 10 to 15 years ago. These secular changes in the growth patterns of children are probably a reflection of better living conditions in Bahrain in recent years. Data on secular trends for growth patterns in certain developed and developing countries have also shown a marked intergenerational increase in body size and a tendency toward earlier sexual maturation as the socioeconomic conditions and nutritional status of populations have improved.[19]

Earlier studies from other Arab Gulf states such as those from Oman and Saudi Arabia[4-6,20] also showed that children in these countries were shorter and lighter than their counterparts in the present study. However, a recent study by El Mouzan et al for the development of reference growth charts of Saudi children and adolescents showed comparable findings for height and weight.[21] The current findings of low height-for-age and normal/high weight-for-height in boys and girls compared to the reference population suggest a genetic control on height. On the other hand, studies are now reporting the possibility of an environmental control. Becker and his colleagues propose that the important association between stunting and high weight-for-height in a variety of ethnic, environmental and social backgrounds is possibly a consequence of nutritional insults during pregnancy and infancy that have long-term effects on a wide range of metabolic and other relationships.[22] Although the underlying mechanisms remain unexplained, this biological phenomenon could raise public health concerns in countries experiencing nutrition transition and changes in activity pattern.

Compared to NCHS/WHO reference standards the distribution of BMI was positively skewed for Bahraini

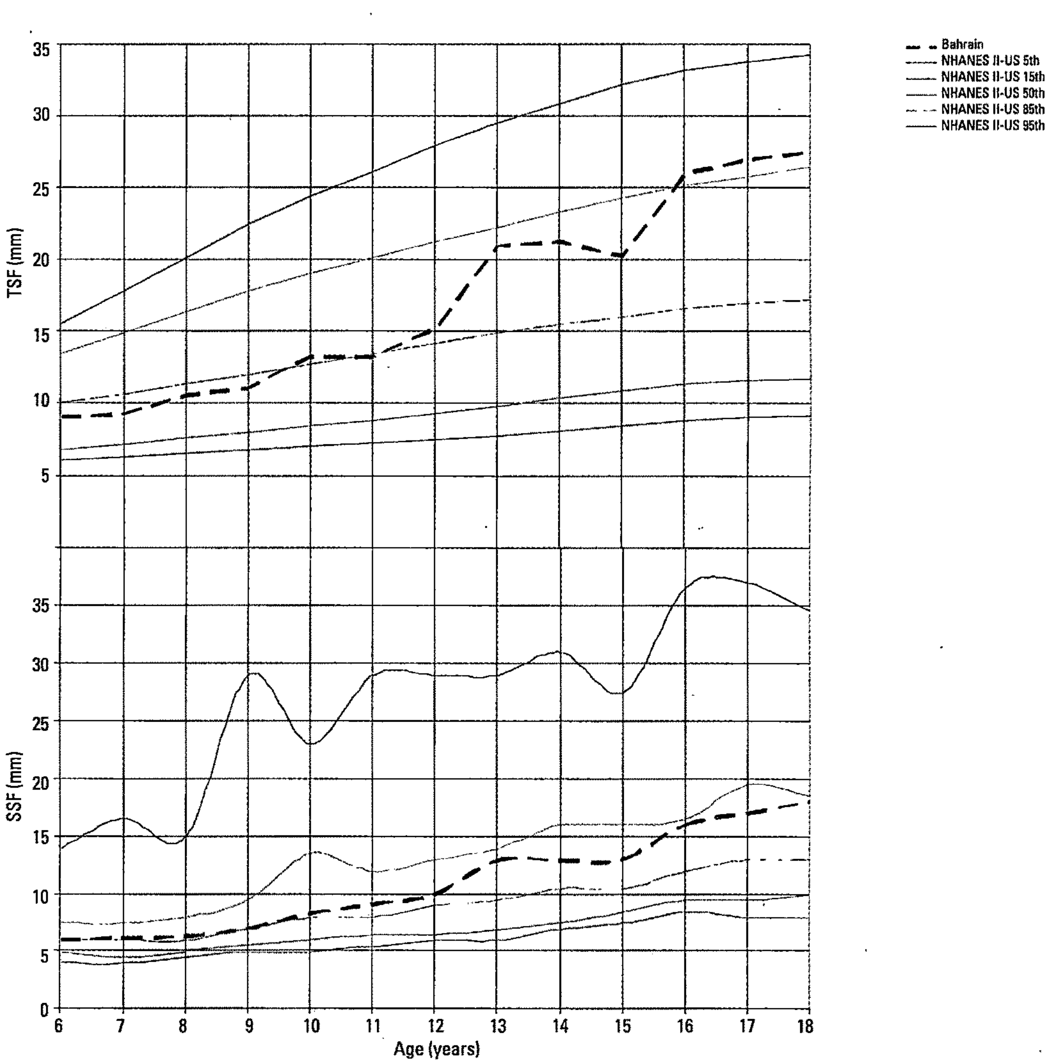

Figure 3. Median triceps skin fold thickness (TSF) and subscapular skin fold (SSF) thickness by age in girls compared to NHANES II-US (5th, 15th, 50th, 85th, 95th percentiles).[16]

girls during adolescence, indicating a trend toward overnutrition in this age group. These observations are in line with the high BMI distributions seen among Bahraini women (≥19 years) in a recent national nutrition survey (2000).[23] Flegal and Troiano[24] in the US suggested that the causes for widespread obesity lie mainly at the population level with social and environmental factors playing an important role. Better socioeconomic circumstances in transitional societies generally leads to increased availability of food, changes in food composition and patterns of food intake, less time spent on physical activity and perhaps also changes in cultural and social attitudes and values that directly or indirectly affect body weight. All these factors exist in this region and might explain, to a large extent, the high prevalence of overweight and obesity.[23,25]

Current findings also show that the BMI cut-off value for overweight status (85th percentile) is higher than that of the WHO reference especially during adolescence. Hence, use of the WHO charts is likely to show exaggerated prevalence estimates of overweight/obesity in Bahraini children. We suggest that local reference standards be developed for Bahraini children and adolescents.

Compared to findings of earlier studies from Bahrain and Saudi Arabia,[3,4] the current generation of Bahraini children show substantially higher values in arm circumference size. Assessment of mean AMA values of current Bahraini adolescents were close to observations made by a recent local study,[26] but lower than those reported for American and German boys and girls of cor-

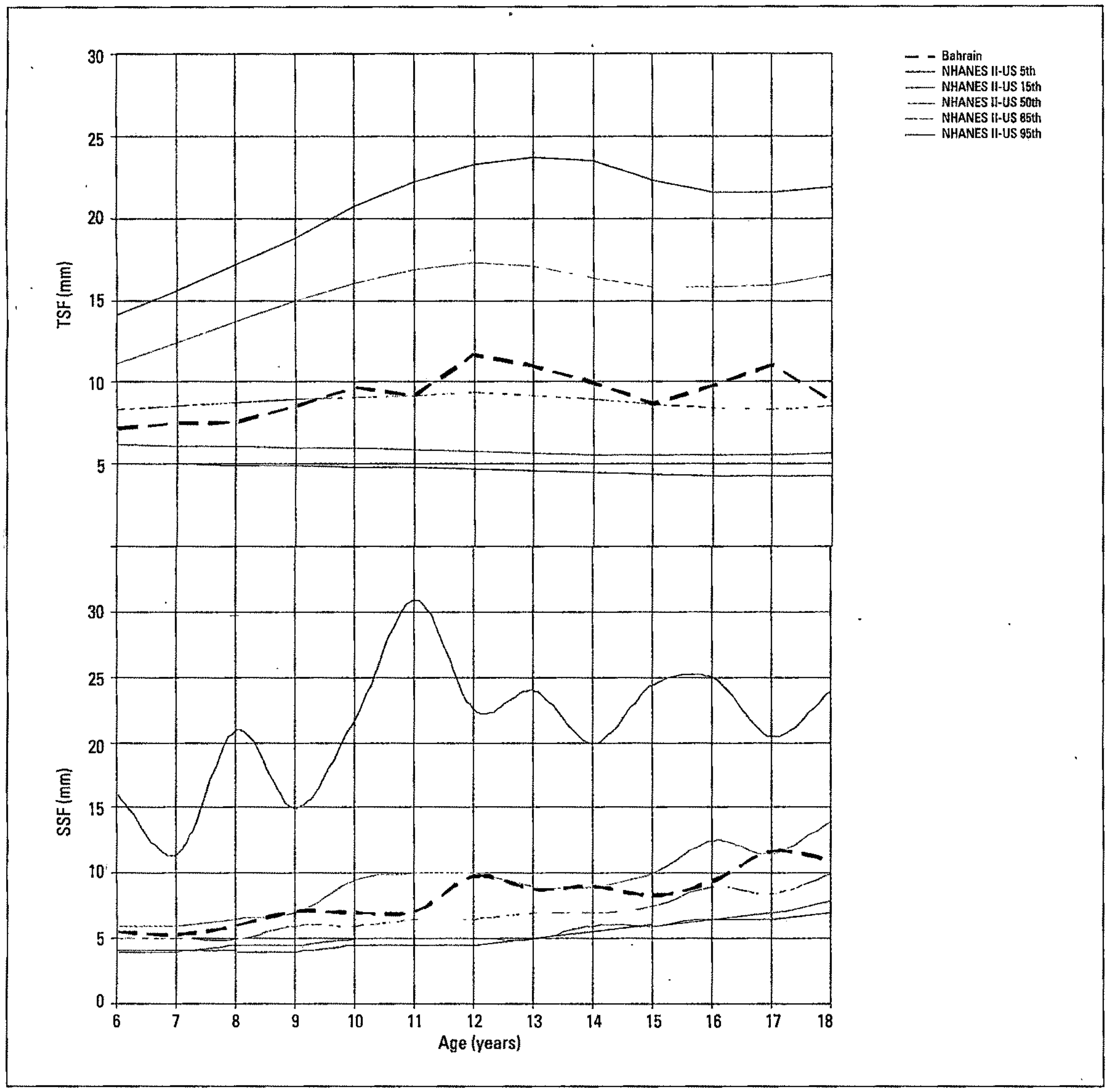

Figure 4. Median triceps skin fold thickness (TSF) and subscapular skin fold (SSF) thickness by age in boys compared to NHANES II-US (5th, 15th, 50th, 85th, 95th percentiles).[16]

responding ages.[16,27] This variation in muscularity with Western children may be due to differences in genetic as well as environmental factors such as level of physical activity related to use of arms and/or variations in dietary patterns. A lower AMA among girls than boys is perhaps a consequence of greater sedentarism among girls of this region as well as physiological causes.[28]

Measurement of skin fold thicknesses, as a specific index for obesity, has some advantage over the weight-for-height.[29] While high weight-for height may be due to excessive muscularity as found in athletes, skin fold thickness provides an indirect estimate of total body fat. Current TSF thickness findings indicate a higher accumulation of body fat in the arms of Bahraini vs. US children. Median TSF thickness Bahraini values were also higher than those of children from the UK (7-10 years of age),[30] Germany (6-18 years of age),[27] and Mexico (5-9.9 and 10-17.9 years of age).[28] Compared to findings of surveys conducted in this region a decade ago[3,4] current values for skin-fold thicknesses (TSF and SSF) were much higher, indicating the rising secular trend of overnutrition. A recent study[1] reported higher values for TSF thickness in Bahraini adolescents than found in our study. This difference is probably due to variation in the type of skin-fold measuring calipers used. Whereas we used the Harpenden calipers, Al-Sendi et all used the Holtain and Lange calipers. Variation in measurements have

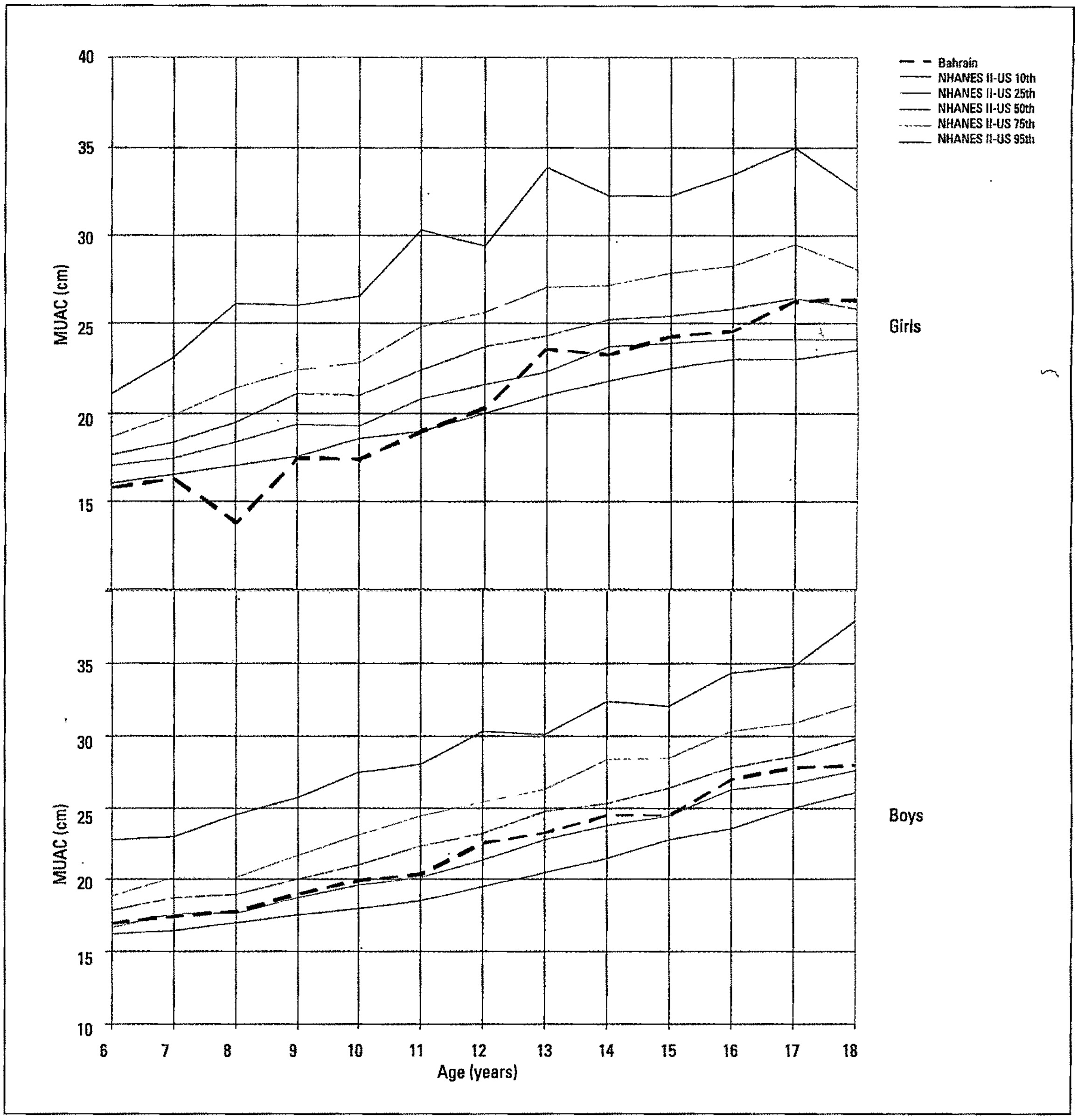

Figure 5. Median mid-upper arm circumference (MUAC) for boys and girls compared to NHANES II US standards (10th, 25th, 50th, 75th, 95th percentiles).[15]

been reported in individuals with the use of different types of calipers.[18]

Median SSF thickness values in Bahraini children were also higher than those of American children (NHANES-II) during adolescence. Both total body fat and regional fat deposition in childhood or adolescent obesity have been associated with adult disease.[31] Researchers have pointed that children with both high BMI and trunk skin fold values have an increased risk of centralized obesity in adult age, which in turn has an increased risk of cardiovascular disease.[32] Moreover, centralized or upper body fat in children carries an increased risk for metabolic complications, such as increased levels of plasma low-density lipoprotein cholesterol, triglycerides, basal insulin and low levels of high density lipoprotein cholesterol.[33-35]

The findings of the present study on BMI as well as on TSF and SSF thickness suggest an increased trend for adiposity among Bahraini adolescents, especially in girls, which puts this age group at a higher risk of adult obesity and its consequences. A need for urgent intervention programs is emphasized.

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original article

Factors associated with sexual dysfunction in Jordanian women and their sexual attitudes

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Ann Saudi Med 2009; 29(4): 270-274

BACKGROUND: Female sexual dysfunction (FSD) is defined as disorders of libido, arousal, and orgasm, as well as sexual pain, that leads to personal distress or interpersonal difficulties. Social aspects of FSD have been understudied. The aim of this study was to explore the social aspects of FSD and sexual attitudes of Jordanian women.

SUBJECTS AND METHODS: Six hundred thirteen married females were studied between October 2006 and August 2007 at the National Center for Diabetes, Endocrinology and Genetics (NCDEG), Amman, Jordan. Females were interviewed using a special questionnaire that was suitable to our culture and added to the Arabic translation of the Female Sexual Function Index (FSFI) Questionnaire.

RESULTS: Older age was associated with a decreased total FSD index and its domain scores. Women with obesity were more likely to have impaired arousability and impaired capability of reaching orgasm. About 58.5% of women reported that they prepared themselves if they had sexual desire and 68.2% reported wearing special attire for this purpose. Only 37.2% of women could ask their husband for a special excitement.

CONCLUSIONS: FSD is prevalent in Jordan. Its social aspects are understudied and need more research in the future.

Sexuality is an important part of health, quality of life and general well being.[1] Sexual dysfunction impacts significantly on a women's self-esteem and quality of life and causes emotional distress, leading to relationship problems.[2,3] Previous studies showed that the prevalence rates of sexual dysfunction among all women ranged between 25% and 63%.[4-6] In postmenopausal women, the prevalence of sexual dysfunction varied from 68% to 86.5%.[7,8] Relatively little research has focused on the social factors that are associated with sexual dysfunction and the sexual attitudes of women.

Islam is a religion that esteems women and places importance on the marital relationship and foreplay in achieving satisfaction. Aspects like preparation for coitus and proper knowledge about marital relationships before getting married are integral parts of Islamic behavior.[9] Data on sexual behavior and sexuality among women in Islamic countries are sparse. This study aimed to address the social aspects of sexuality among Jordanian women and determine factors associated with sexual dysfunction.

SUBJECTS AND METHODS

A systematic random sample of 613 married women was selected from all females who attended the National Center for Diabetes, Endocrinology and Genetics (NCDEG) in Jordan between October 2006 and August 2007. In systematic random sampling, first a number within the sampling interval was chosen. We chose a random number between 1 and 10 using random number tables. Then every 10th woman following the first number chosen was selected each day for the whole study period. Divorced, widowed or seriously ill women were excluded from the study. This study was approved by the NCDEG ethics committee. Participants were informed about the objective of the study, and asked to read carefully and sign a consent form, which was also approved by the ethics committee. All women agreed to participate in this study and signed the consent form. A face-to-face interview was held by a female researcher while assuring privacy and confidentiality to collect data. Demographic and clinical data were recorded. Women were asked to answer selected culture-sensitive questions (Appendix 1) to assess their behaviors and attitudes toward sexual functioning. In addition, the structured interviews were based on the 9-items of the Female Sexual Function Index (FSFI) Questionnaire,[10] which was translated to Arabic, and tested for validity and reproducibility. Scores of the six domains, which included desire, arousal, lubrication, orgasm, satisfaction and pain, were added to obtain the full-scale score. For individual domain scores, scores of the individual items that comprise the domain were multiplied by the domain factors, where higher scores indicate less dysfunction.[10]

Weight and height were measured while the subject was wearing light clothes and not wearing shoes. Weight was taken to the nearest 0.5 kilogram and height was taken to the nearest 0.5 centimeter. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Females were categorized as being of normal weight (BMI<25 kg/m^2), overweight (BMI=Age and body mass index 25-29.9 kg/m^2), or obese (BMI≥30 kg/m^2).

The Statistical Package for Social Sciences software (SPSS, version 15, Chicago. Inc) was used for data processing and data analysis. Characteristics of subject variables were described using frequency distribution for categorical variables and mean and standard deviation for continuous variables. The multivariate analysis of the association between FSFI domains and independent variables was conducted using the general linear model multivariate procedure. This procedure provided regression analysis and analysis of variance for multiple dependent variables (FSFI domains) by explanatory variables and covariates. A *P* value of less than .05 was considered statistically significant.

RESULTS

About half (47.8%) of the 613 women were younger than 50 years, 35.2% were between 50 and 59 years , and 17% were 60 years or older. Only 10.2% of women had a BMI<25 kg/m^2, 31.9% were overweight and 57.9% were obese. In the multivariate analysis, older age was associated with decreased total FSDI scores and its domains scores (Table 1). Compared to those with normal BMI, obese subjects were more likely to have impaired arousability and impaired capability of reaching orgasm.

About 41.1% of women considered their kids the most important person in their lives, while only 33.8% considered their husbands as the most important. When they were asked to identify factors that might hinder their sexual functioning, 23% identified lack of water, 24.1% identified lack of privacy and 36.4% identified kids being awake at night as the most important factors. About 51.3% of women reported that they keep themselves neat on a daily basis during time spent at home and only 54.3% keep themselves neat for their husbands return from work. This is compared to 61.7% of women who reported that they keep themselves neat for a women's gathering. About 58.5% of women reported that they prepare themselves if they have sexual desire and 68.2% reported wearing special attire for this purpose. About 67.1% of females reported that they keep themselves ready if they feel that their husbands have sexual desire. As for Friday (weekend) night, it was considered a special night for 28.4% of women, where 44.8% of them wear special clothes, 40.1% put on makeup and 46.3% use a special perfume. Only 37.2% of women could ask their husband for a special

Table 1. Multivariate analysis of factors associated with total female sexual dysfunction index by domain scores.

Variable	Desire	Arousal	Lubrication	Orgasm	Satisfaction	Pain	Total
Age (years)							
<50	3.6 (1.4)	3.6 (1.6)	4.3 (1.6)	4.1 (1.7)	4.2 (1.5)	2.6 (1.2)	22.7 (7.4)
50-59	3.0 (1.5)	3.0 (1.7)	3.6 (2.0)	3.5 (2.0)	4.0 (1.8)	2.4 (1.4)	19.8 (8.8)
≥60	2.5 (1.4)	2.5 (1.7)	2.9 (2.1)	2.9 (2.1)	3.6 (1.8)	1.9 (1.2)	16.6 (8.9)
P value	.0001	.0001	.0001	.0001	.087	.0001	.0001
Body mass index							
Normal	3.5 (1.5)	3.4 (1.6)	4.1 (1.7)	4.0 (1.7)	4.1 (1.6)	2.7 (1.2)	22.1 (7.6)
Overweight	3.3 (1.5)	3.4 (1.7)	3.9 (1.9)	4.0 (1.9)	3.9 (1.7)	2.2 (1.1)	21.2 (8.7)
Obesity	3.1 (1.5)	3.1 (1.7)	3.7 (1.9)	3.5 (1.9)	4.1 (1.7)	2.5 (1.3)	20.3 (8.4)
P value	0.055	0.036	0.165	0.005	0.723	0.242	

excitement and 36.8 % of them would ask for a specific sexual position. About 84.6% reported being kissed before coitus, 83.4% during and 51.9% after finishing intercourse.

DISCUSSION

Sexual attitudes differ between different societies, among different eras, between different individuals and even in the same person when times and circumstances change.[3] Sexual intercourse is not the only component of a marital relationship.[3] It is emotional sharing and mutual sentiments that culminate in intercourse, preceded by sufficient foreplay that leads to satisfaction and pleasure in both the man and woman.[3] The importance of foreplay is underscored and recommended strongly in Islam and it is mentioned in the holy Quran and the Hadith (Table 2). For foreplay to take place, the elements of preparing oneself via cleanliness and having a pleasant odor should be present. This applies to both husband and wife.[3] For the wife to put on special clothes, wear perfume and makeup-if desired-are suitable anticipatory actions that are encouraged because they pave the way for a successful encounter.[3] There are no restrictions as far as kissing and talking during coitus. In fact that is stressed in Islam but, unfortunately, ignored in some cultures because of misconceptions or traditions. The same applies for postcoital kissing and cuddling. There are no borders between a husband and wife as far as the position or kind of excitement desired during intercourse,[3] a fact that is also shadowed by traditions and misconceptions.

In our study, the issue of the mutual respect and treatment between man and woman had an impact on FSD, which goes back to the core of Islam emphasizing the essentiality of treating women well and the fact that the emotional and psychological aspects of marital relations are as important as the physiological ones.[3] Keeping themselves neat and at times tempting only for the husband, as required in Islam, was not the trend of the women in our study, who kept themselves neat for outside visits and women's gatherings more than for the husband at home. Nonetheless, not few were those women who were aware of Islamic teachings of preparing oneself for the husband if they or their men had the desire for marital relations. Kissing and cuddling were integrated into the marital relations, before and during coitus to a larger extent than after, which shows an awareness of Islamic behaviour. This is in accord with the Hadith which stressed the kiss as the best messenger in foreplay. However, this did not apply to aspects of position and special excitements during coitus, which few women could ask for.

Table 2. Passages from the holy Quran.

> *"Your wives are as a tilth unto you so approach your tilth when or how ye will; but do some good act for your souls beforehand and fear Allah, and know that ye are to meet him (in the thereafter), and give (these) good tidings to those who believe* (The holy Quran, Al Baqara, verse 223)."
>
> *"Permitted to you on the night of the fasts, is the approach to your wives. They are your garments and ye are their garments. Allah knoweth what ye used to do secretly among yourselves, but he turned to you and he forgave you, so now associate with them, and seek what Allah hath ordained for you , and eat and drink until the white thread of dawn appears to you distinct from its black thread; then complete your fast till the night appears; but do not associate with your wives while ye are in retreat in the mosques. These are limits (set by) Allah; approach not night thereto. Thus doth Allah make clear his signs to men: that they may learn self- restraint* (The holy Quran, Al Baqara, verse 187)."

Our findings that age and BMI have a negative impact on female sexual function are in accord with other studies[6,7] but in contrast to the study of Enzlin and associates, in which no association was found between age, BMI and FSD.[8]

In our study, females holding a diploma degree had FSD more than others. Higher education level was associated with more FSD in the study of El Nashar et al.[4] The higher incidence of sexual dysfunction in better educated individuals is surprising given that they are healthier and have lifestyles that are less physically stressful and emotionally demanding. However, a higher educational level may also be associated with an increase in ability to freely express their dissatisfaction.[4] This finding agrees with those of van Gleen et al,[9] who showed a positive correlation between level of education and sexual dysfunction. In our study, female employment had a significant impact on FSD , in contrast to the findings of El Nashar et al.[3] Privacy was an issue in FSD in our study as well as in the study of El Nashar et al.[3] Nonetheless, socioeconomic status did not have a significant impact on FSD, which is in accord with the findings of El Nashar et al,[4] but in contrast to the findings of Laumann et al.[10]

The records of the Jordanian Islamic courts have an estimate of 13% for polygamous marriages (for the years

2002 to 2006) in comparison to 10.7% in our study, bearing in mind that the court records are more accurate because in reality some women do not know that their husbands are married to other women. Nonetheless, and as far as we know, there were until now no studies that addressed issues of polygamy and FSD, and other social aspects of the issue, such as the effect of the mode of marriage on FSD and female preparation for coitus. The frequency of polygamy and related factors needs further study. One of the shortcomings of the study is that only women were interviewed and some issues require the opinion of the husband. Studies involving couples would be good in the future.

In conclusion, FSD is prevalent in Jordanian females and the sexual attitudes of these women need to be explored in more detail in future research.

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- If you were to choose the most important person in your life in terms of priority, it would be: yourself, your husband, your parents (mother, father, both), your kids (males, females, both),others (brothers, sisters, others).
- Is your husband married to another woman?
- Does the lack of water (hot water specifically) constitute a problem?
- Is lack of privacy a problem?
- Does the presence of kids and their number (especially if they stay awake late at night) constitute a problem?
- Did you have information about marital life prior to getting married?
- If yes, did you get information from: mother, female friends, books, magazines, films?
- Was your marriage traditional or by love?
- If traditional, was it to a non-relative? First-degree cousin? Second-degree cousin?
- Do you remember your weight at marriage?
- When did your weight start to increase? After marriage? After your first kid?
- Do you keep yourself neat on daily basis while at home?
- Do you keep yourself neat if your husband comes and tells you he's coming home?
- Do you prepare yourself if your husband is taking you out?
- Do you prepare yourself if you're going out for a women's meeting?
- Do you prepare yourself if you had desire for marital relation?
- Do you wear special clothes if you had a desire for sex?
- Do you prepare yourself if you feel your husband wants to have sex?
- Do you wear special clothes to seduce your husband if you had the desire for a marital relation?
- Is Friday night considered a special day to you? (Do you wear special clothes then? Special makeup? Special perfume?)
- Was your husband nicest in his twenties, thirties, forties, fifties, sixties, or he did not change all through?
- Can you ask your husband for any special excitement during sex?
- Can you ask your husband for a special position during coitus?
- Does your husband kiss you in general?
- If yes, as he comes in home? as he comes from travel ? before coitus? During or after coitus?

Appendix 1. Special questionnaire used to assess the social aspects of female sexual dysfunction.

original article

Prevalence of psychological symptoms in Saudi Secondary School girls in Abha, Saudi Arabia

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Ann Saudi Med 2009; 29(4): 275-279

BACKGROUND AND OBJECTIVES: Adolescence is characterized by rapid physiological, social and cognititive changes. Aim of the present work is to study mental health of Saudi adolescent secondary school girls in Abha city, Aseer region, Saudi Arabia.

METHODS: A cross-sectional study was conducted in 10 secondary schools for girls using the Arabic version of the symptom-revised checklist 90 (SCL 90-R), a mental health questionnaire that was administered to the girls by fourth-year female medical students.

RESULTS: The most prevalent mental symptoms in the 545 female students were phobic anxiety (16.4%), psychoticism (14.8%), anxiety (14.3%), and somatization (14.2%). The prevalence of depression, paranoid ideation and interpersonal sensitivity amounted to 13.9%, 13.8% and 13.8%, respectively. The least prevalent mental symptoms were hostility (12.8%) and obsessive-compulsive behavior (12.3%). Overall, psychological symptoms (in terms of a positive global severity index) were found in 16.3% of the girls. In a multivariate logistic regression analysis, no significant relationship was found with sociodemographic factors.

CONCLUSION: Psychological symptoms and disorders are prevalent in secondary school girls and health professionals need to be able to recognize, manage and follow-up mental health problems in young people. Further research is needed to explore the magnitude of the problem at the national level.

Adolescence (11 to 19 years of age) is characterized by rapid physiological, social and cognitive changes.[1] Poor mental health during this period has been linked to mental health problems in adulthood.[2] Worldwide, about 16% of adolescents suffer from mental health problems.[3] In the United States, the direct cost of mental health services accounted for 69 billion US dollars, which represents 7.3% of total health spending.[4] However, mental health promotion may help to prevent a wide range of health-damaging behavior as well as improving the quality of life of young people.[5] In the United States, about 20% of children and adolescents are estimated to have mental health disorders.[6] In Canada, 9.5% of boys and 12% of girls have mental health problems.[7] Reports from India have estimated the prevalence of mental disorders from 2.6% to 35.6%.[8] In the neighboring country of the United Arab Emirates, 22.2% of children aged 6 to 18 years were reported to have mental health problems.[9] A large proportion of the population of Saudi Arabia is young, with 69% under 30 years old, and 47% under 15 years.[10] However, there is a general paucity of research in the area of adolescent mental health. A recent study of boys in secondary school (age range from 15-18 years) in Abha city reported that more than one-third (38.2%) had depression, while 48.9% had anxiety and 35.5% had stress.[11] Like other countries, adolescent girls in Saudi Arabia face rapidly changing challenges in their social and physical environment.[5,7-9] Therefore, the purpose of this study was to estimate the prevalence of mental health symptoms among secondary school girls in Abha City in southwest Saudi Arabia and to assess related sociodemographic characteristics.

METHODS

This cross-sectional study was conducted during the 2006-2007 scholastic year in Abha. The subjects were girls in secondary school (representing the tenth, eleventh and twelfth years of general education in Saudi Arabia, which starts at 7 years of age). Abha is the capital city of the Aseer region in the southwest of Saudi Arabia, with a total population of 300000. In Saudi Arabia, schools for girls are segregated from boys.

The city has a total of 10 secondary schools for girls, including 7 general schools and 3 Islamic (Tahfez Al-Quran) schools. All information about the study was provided to schools through the Abha School Health unit. All schools agreed to participate in the study. Field activities were conducted by trained fourth-year female medical students who were supervised by the staff of the Family and Community Medicine Department, College of Medicine, King Khalid University. Two classes were randomly selected from each school (first, second and third year).

The purpose of the study was explained to the participants in the classrooms. All students were clearly informed that they could choose not to participate. Subjects were assured of anonymity and confidentiality. All students in the selected classes during the study period were considered for inclusion in the study. Signed informed consent was given by each participant student.

The mental health questionnaire was based on the Arabic validated version of the Symptoms Check List 90-revised (SCL 90-R) questionnaire.[12] This scale is used extensively to screen for mental health symptoms.[13] The SCL 90-R test is a self-reporting instrument intended to measure severity of psychiatric symptoms on a number of different subscales. It contains 90 items and can be completed in just 12 to 15 minutes. Students rated the 90 symptoms of distress on a 5-step Likert-scale with 0 being 'not at all' and 4 being 'extremely'. Subjects were instructed to indicate the amount they were bothered by each of the symptoms during the preceding week. Relevant dimension scores were summed and the 't' transformation of the scores was performed. The positive dimension was considered when relevant *t* scores were 61 or more. The test helps in measuring nine primary symptom dimensions and three global indices of distress. It is designed to provide an overview of symptoms and their intensity at a specific point in time. The dimension includes somatization (the process by which psychological needs are expressed in physical symptoms), obsessive-compulsive (a form of personality marked by obsessions and compulsions), interpersonal sensitivity (relating to a conflict in the relations and social exchanges between persons), depression (a mental state of depressed mood characterized by feelings of sadness, despair and discouragement), anxiety (the unpleasant emotional state consisting of psychophysiological responses to anticipation of unreal danger), hostility (tendency to feel anger toward and to seek to inflict harm upon a person or group), phobic anxiety (fear that is recognized as being excessive or unreasonable by the individual himself), paranoid ideation (persistent delusions of persecution or delusional jealousy and behaviour such as suspiciousness, mistrust and combativeness), and psychoticism (a person will exhibit some qualities commonly found among psychotics such as disregard for common sense).[14] The three global indices are Global Severity Index (GSI), Positive Symptom Distress Index (PSDI) and Positive Symptom Total (PST). GSI is designed to measure overall psychological distress. PSDI is designed to measure the intensity of symptoms. The PST reports the number of self-reported symptoms.

Statistical analysis was conducted using the SPSS version 15. All tests were carried out at the 5% level of significance. A multivariate logistic regression analysis was used to identify potential sociodemographic risk factors that might affect mental symptoms. Adjusted odds ratio and concomitant 95% confidence intervals were calculated.

RESULTS

Five hundred and forty-five Saudi secondary school girls were included in the present study (Table 1). Their ages ranged from 14 to 19 years with a mean (SD) of 17.1 (1.1) years and a median of 17 years. Twenty students (3.7%) were married. Their ages ranged from 16 to 19 years. The majority (89.0%) had parents living together. The rest had separated (0.2%), divorced parents (4.2%) or a deceased father or mother (6.6%). The most frequent level of education among fathers was a university education (39.4%), while 7.9% were illiterate. On the other hand, the mothers' education was most often primary (29.9%), followed by none (28.3%). The most frequent occupation of fathers was as a military or governmental employee (46.0%). Most mothers were not working (87.9%). The majority of students (74.35%) were from families whose family size ranged from 5 to 10 persons. The average monthly family income ranged from 5000 to 10 000 Saudi Riyals (SR) (1 US dollar equals 3.75 SR) in 47.5% of the study sample. The remainder were either below 5000 or above 10 000.

Table 2 shows the overall prevalence of mental symptoms among adolescent secondary school girls. The most frequent mental symptoms were phobic anxiety (16.4%), psychoticism (14.8%) and anxiety (14.3%). The least frequent dimensions were obsessive-compulsive behavior (12.3%) and hostility (12.8%). Some students had more than one symptom. Forty-nine girls (9.0%) had simultaneously 2 symptoms, 31 girls (5.7%) had 3 symptoms and 24 girls (4.4%) had 4 symptoms. Table 3 shows the global indices of distress. The positive global severity index (GSI) amounted to 16.3%, which indicates that at least one out of each of six girls suffers from one or more mental health symptoms. The

Table 1. Sociodemographic characteristics of the secondary school girls.

	No	%
Age		
14-15	22	4
16-17	333	61.1
18-19	190	34.9
Marital status		
Married	20	3.7
Single	525	96.3
Scholastic year		
First year	219	40.2
Second year	163	29.9
Third year	163	29.9
Type of study		
Oslamic (Tahfez Al-Quran)	209	38.3
General	336	61.7
Parents' status		
Living together	485	89.0
Divorced	23	4.2
Separated	1	0.2
Deceased father	28	5.1
Deceased mother	5	0.9
Both parents are deceased	3	0.6
Father's education		
Illiterate	43	7.9
Primary	87	16.0
Intermediate	93	17.1
Secondary	107	19.6
University	149	27.3
Postgraduate	66	12.1
Father's employment		
Unemployed	25	4.60
Military	89	16.3
Governmental employee	162	29.7
Private business	106	19.5
Retired	163	29.9
Mother's education		
Illiterate	154	28.3
Primary	163	29.9
Intermediate	88	16.1
Secondary	69	12.7
University	54	9.9
Postgraduate	17	3.1
Mother's employment		
Housewife	479	87.9
Employed	66	12.1
Family size		
Less than 5	41	7.5
5-10	405	74.3
More than 10	99	18.2
Total	**545**	**100**

Table 1 (cont.). Sociodemographic characteristics of the secondary school girls.

Table 2. Overall prevalencea of mental symptoms among secondary school girls in Abha, Saudi Arabia.

Mental symptom	**Prevalence**[a]	
	No	**%**
Phobic anxiety	90	16.5
Psychoticism	80	14.7
Anxiety	78	14.3
Somatization	77	14.1
Depression	76	13.9
Interpersonal sensitivity	75	13.8
Paranoid ideation	75	13.8
Hostility	70	12.8
Obsessive-compulsive behavior	67	12.3

[a] Categorization was based on "t" transformation of SCL R-90 scores. Positive dimension was considered when "t" scores are 61 or more.

[a] Total is more than 100% as some students have more than one disorder (comorbidity)

Table 3. Positive global indices of distress among secondary school girls in Abha, Southwestern of Saudi Arabia (n= 545).[a]

Positive global indices of distress	**Prevalence (%)**
Global Severity Index (GSI)	16.3
Positive Symptoms Distress Index (PSD)	13.7
Positive Symptoms Total (PST)	14.0

[a] Categorization was based on "t" Transformation of SCL R-90 scores. Positive dimension was considered when "t" scores are 61 or more.

Table 4. Adjusted odds ratio (aOR) and 95% confidence intervals (CI) for potential sociodemographic risk factors that might be associated with the highest three prevalent mental symptoms among secondary school girls in Abha, Saudi Arabia (n=545), by multivariate analysis.

Potential Socio-demographic Risk Factor	Phobic Anxiety	Psychotocism	Anxiety
Age (<17 years vs. ≥17 years)	1.1 (0.6-2.2)	1.1 (0.6-2.2)	1.5 (0.8-3.0)
School (general vs. culture)	0.8 (0.4-1.4)	0.8 (0.4-1.5)	0.6 (0.3-1.2)
Marital status (single vs. married)	0.9 (0.3-3.0)	0.8 (0.2-3.1)	1.8 (0.4-8.3)
Family size (<5 persons vs. ≥5 persons)	0.7 (0.3-1.6)	1.9 (0.6-5.9)	0.6 (0.3-1.4)
Parental status (living together vs. others)	0.7 (0.4-1.9)	1.4 (0.6-2.9)	1.8 (0.9-3.7)
Father education (illiterate vs. educated)	1.4 (0.6-3.3)	1.0 (0.4-2.6)	1.4 (0.6-3.6)
Mother education (illiterate vs. educated)	1.4 (0.8-2.4)	0.6 (0.3-1.1)	0.9 (0.5-1.7)
Father occupation (retired or not working vs. working)	0.8 (0.4-1.3)	1.1 (0.7-2.0)	0.7 (0.4-1.3)
Mother occupation (not working vs. working)	1.1 (0.6-3.3)	1.1 (0.5-1.2)	1.5 (0.8-3.0)
Average family income (<5000 SR vs. ≥5000 SR)	1.1 (0.6-1.9)	1.2 (0.7-2.2)	0.8 (0.4-1.5)

positive symptoms distress index was 13.7% and positive symptoms total was 14.0%.

Table 4 shows multivariate logistic regression analysis of potential sociodemographic risk factors affecting the highest three prevalent mental symptoms: phobic anxiety, psychotocism and anxiety. None of the potential sociodemographic factors (age, type of school, marital status, family size, parental status, parental education and occupation and average of family income) were found to significantly affect the highest three prevalent dimensions of mental health. The same findings were present in the rest of the mental health dimensions.

DISCUSSION

Using a standardized instrument that assesses a broad range of mental health problems, we found that symptoms were prevalent among secondary school girls, with 16.3% suffering from one or more mental health symptoms.

In a previous study conducted on secondary school boys in the same area using Depresion, Anxiety and Stress Scale (DASS) questionnaire, indicated that of 1723 Saudi adolescent school boys, 59.4% had at least one of the three studied disorders (depression, anxiety or stress), 40.7% had at least two and 22.6% had all three disorders. Moreover, more than one-third of the participants (38.2%) had depression, while 48.9% had anxiety and 35.5% had stress. Depression, anxiety and stress were strongly, positively and significantly correlated.[11] Fehan et al reported that 63% of New Zealand adolescents have mental illness.[15] Other studies found rates of 22.2% in United Arab Emirates,[8] 18.5% in USA,[16] 17.9% in Puerto Rico,[17] 22.5% in Switzerland,[18] 9% among boys and 12% among girls in Canada,[6] 8% in India,[7] and 20.3% in Taiwan.[19] The prevalence ranged from 1% to 51% (mean=15.8%) conducted over the last 40 years from 20 countries.[3] This variation could be related to using different measure tools.

The most frequent mental symptoms were phobic anxiety (16.4%), psychoticism (14.8%) and anxiety (14.3%), which is in agreement with the literature that indicates that anxiety disorders are the most common psychiatric diagnosis in adolescents.[20,21] In an earlier study of 1723 male high school students in Saudi Arabia using an Arabic version of DASS, nearly 49% were found to have an anxiety disorder.[11] Studies indicate that females have a higher prevalence of anxiety.[7,22] On the other hand, the least frequent dimensions in this study were obsessive-compulsive (12.2%) and hostility (12.9%). In the UAE, Eapen et al reported that 7% and 9% of adolescents have phobia and anxiety, respectively.[8] Fehan et al found that in New Zealand, anxiety and simple phobia were present in 65% and 41%, respectively.[15]

The majority of students came from families that ranged in size from 5 to 10 persons, which is in agreement with the average Saudi family size reported in previous research.[10] About two-thirds of mothers had either a primary education (29.9%) or were illiterate (28.3%). Unlike our finding, Brandon found that children whose mothers are employed were more likely to have emotional problems which can be secondary to the differences. Average family income was less than 5000 SR in 21.8%. However, this did not significantly affect the nine dimensions of mental health. Neither did other potential sociodemographic risk factors (age, school type, marital status, family size, rank among brothers and sisters, parental status, parental education and occupation and average monthly family income (Table 4). A risk factor does not necessarily imply a direct causal relationship. It has been reported that emotional problems are most likely to be due an interaction between biological and environment factors.[24] Integration of mental health into medical setting might improve care and reduce stigmatization of mental illness.[25] Primary health care centers care offer a setting for the prevention and detection of mental health problems in adolescents. Further research is needed to determine the magnitude of psychiatric disorders at national level.

The questionnaire used in this study had the advantage of being psychometrically validated and developed in consideration of cross cultural and linguistic issues. However, this study has some limitations: it was restricted to female adolescents, which led to an inability to determine sex-specific psychopathology. Since it was a school-based study, it might miss adolescents in the community who do not attend schools. However, the results would reflect the state of psychopathology among adolescents.

In conclusion, the high prevalence of mental symptoms represents one of the major health problems affecting adolescents in Abha city. Further in-depth studies are needed to study mental disorders in the area and to identify potential supporting counseling and cognition-behavior therapy. In this context, a national program for mental health in this age group is crucial.

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original article

Accuracy of the Fischer scoring system and the Breast Imaging Reporting and Data System in identification of malignant breast lesions

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Ann Saudi Med 2009; 29(4): 280-287

BACKGROUND AND OBJECTIVES: Fischer developed a scoring system in 1999 that made identifying malignant lesions much easier for inexperienced radiologists. Our study was performed to assess whether this scoring system would help beginners to accurately diagnose breast lesions on magnetic resonance (MR) imaging and to assess the correlation between the magnetic resonance mammography Breast Imaging Reporting and Data System (MRM BI-RADS) grade and the final diagnosis.

PATIENTS AND METHODS: The lesion morphology and contrast kinetics of 63 masses in 41 patients were evaluated on MRI and accorded a MRM BI-RADS final assessment category using the Fischer scoring system. The accuracy was evaluated after the final diagnosis was obtained by tissue sampling and follow-up imaging.

RESULTS: There were 25 malignant and 30 benign lesions. Eight lesions were seen by MRI only and we could not verify their pathology since we did not have MR-guided biopsy facilities at the time of the study. On MR mammography, the proven carcinomatous lesions were characterized as BI-RADS category V in 16 (64%), category IV in 7 (28%), and category III in 2 (8%) lesions. Benign lesions were graded as category V in 3 (10%), category IV in 6 (20%), and category III in 3 (10%), category II in 10 (33%) and category I in 8 (27%) lesions. The MRM BI-RADS category accurately predicted malignancy in 92% and a benign pathology in 70% of the lesions. The overlap between the MRM features of chronic inflammatory lesions and carcinomas resulted in a lower accuracy in diagnosing benign as compared to malignant lesions.

CONCLUSION: The MRM BI-RADS lexicon using the Fischer scoring system is useful and has a high predictive value, especially for malignant breast lesions, and is easy to apply. Overlapping features between benign inflammatory and malignant lesions might yield a reduced accuracy in inflammatory pathologies.

Breast magnetic resonance imaging (MRI) is extremely sensitive in the detection of carcinoma, with a sensitivity ranging from 97% to 100%.[1] The specificity is somewhat lower, ranging from 50% to 80% as reported previously.[2,3] The wide range of specificity may be due to the fact that investigators at different institutions use a variety of MR imaging techniques for acquiring and processing images and possibly use different criteria for interpretation. This may also be partly due to differing levels of experience with MR mammography. Given these limitations when interpreting a study, it is important for a radiologist to determine which lesions are suspicious of malignancy and need to be biopsied. A standardized terminology has been developed to facilitate the interpretation and communication among physicians in the description of morphologic findings on mammography. The Breast Imaging Reporting and Data System (BI-RADS),[4] in the form of a lexicon, that is widely used in the United States, was implemented in our hospital a few years back. It is now the standard for reporting conventional x-ray mammograms and uses descriptors to attach a level of suspicion to a lesion and its need for a biopsy. The same lexicon can be used for reporting MRI breast.[4]

The use of morphologic criteria has been shown to improve specificity when used to describe breast findings on MRI.[5,6] For example, smooth or lobulated margins on MRI show a 97% to 100% predictive value for benignity, whereas the presence of rim enhancement shows a 79% to 92% predictive value for malignancy.[5] Despite these encouraging results, the value of morphologic criteria to describe MRI-detected breast lesions has been limited by the lack of a definitive classification scheme.

In 1999, Fischer et al[1] developed a scoring system to predict the likelihood of a lesion on MRI as being benign or malignant. After the magnetic resonance mammography (MRM) BI-RADS classification system (that mirrors the mammographic BI-RADS categories) was described in 2003 by the American College of Radiologists (ACR),[4] we found that the Fischer scoring system made identifying the BI-RADS category much easier for inexperienced radiologists. Our study was performed to assess whether this scoring system would help beginners to accurately diagnose breast lesions on MR imaging and to assess the correlation between the MRM BI-RADS grade and the final diagnosis.

PATIENTS AND METHODS

In this single center prospective study conducted in a breast unit of a general hospital, 41 consecutive cases with identified breast lesions on mammography presenting during the period May 2005 to September 2006 underwent an initial dynamic MR mammography of the breast with follow-up imaging studies as required up to 2 years. The study was conducted using a 1.5T magnet (GE Excite, South Carolina, USA) and the patients constituted part of our initial experience with MR mammography.[7]

The patients included in our study were referred to our MR imaging suite with breast lesions for the following reasons:

1. Equivocal findings on mammography (n=18),
2. Suspicion of local relapse in treated breast cancer patients (n=6),
3. Search for a primary breast cancer in patients with metastatic axillary lymph nodes with suspicious lesion on mammography (n=5),
4. Local staging of breast cancer (suspicion of multiple lesions at standard imaging, dense breasts) (n=5),
5. Differentiation between inflammatory benign lesions vs. inflammatory carcinoma (n=4),
6. MRI screening in high-risk patients with lesion suspicious for cancer on mammography (n=3).

We analyzed the morphologic characteristics, enhancement pattern and kinetic features of the lesions and assigned an appropriate final assessment BI-RADS category (Table 1). The aim of the study was to assess whether the descriptive terminology and final assessment categories of the BI-RADS lexicon using the Fischer scoring system[1] corresponded to the final diagnosis of the lesions as obtained from histopathological confirmation or follow-up.

Patient preparation and positioning

A 20-gauge intravenous line was inserted at the dorsum of the hand before positioning the patient on the table to ensure lack of movement between scans. The MRI breast was performed with the patient lying in a prone position on a platform placed in the MR imager that allows the breasts to be in a dependent position. A dedicated 4-channel breast coil was used. MRI was performed during days 6-16 of the menstrual cycle or after stopping hormone replacement therapy for 4-6 weeks to avoid false positive enhancing lesions during the peak hormonal level of the cycle. If the MRI was requested for suspected recurrence of malignancy, the MRI study was performed 6-8 weeks post surgery and at least 9 months (preferably 12 months) post radiotherapy.

The protocol

Axial T1W 3D SPGR volume images (slice thickness 4 mm, 44 loc per slab, FOV 30, matrix 416×256, NEX 1, flip angle 35, bandwidth 41.67) and sagittal fat-saturated T2W 2D FRFSE images (slice thickness 5 mm, space 1 mm, FOV 36, matrix 320×224, NEX 3, TE 85, TR 5625, echo train length 16, bandwidth 22.73) were obtained prior to contrast injection. Either sagittal or axial fat-saturated T1W high-resolution 3D SPGR dynamic images using vibrant software (slice thickness 4 mm, 66 loc per slab, matrix 256×160, NEX 1, flip angle 12, bandwidth 31.25, ZIP 2 with effective slice thickness of 2.0 mm) were then obtained with a scan time not exceeding 60 sec per scan. Seven acquisitions were obtained simultaneously of both breasts. The first acquisition was obtained before contrast was injected and was used as a mask and the other 6 acquisitions were obtained following contrast injection. The post-contrast acquisitions were finished within 6 minutes. The contrast used was 0.1 mmol/kg of gadolinium-DTPA intravenously, usually injected as a bolus using an automatic injector at a rate of 2mL/sec, followed by a saline flush. The last sequence obtained post contrast was a high T1W spatial resolution sequence; axial 3D SPGR volume fat saturated T1 (slice thickness 4 mm, 44 loc per slab, FOV 30, matrix 416×256, NEX 1, flip angle 35, bandwidth 41.67) which was done at almost 7-8 minutes post contrast.

Image interpretation

The morphology of the lesion was studied on the 3D volume T1W images, the fat saturated post contrast 3D volume T1W images and the fat saturated T2W images and images obtained post-processing (maximum intensity projection and maximum slope of signal increase). The form, margin and the enhancement pattern of the lesions were identified and scored points as in Table 1.

Table 1. Criteria for evaluating breast lesions on contrast-enhanced MR images (the evaluation score).

	Criterion	Points
1	**Shape of contrast-enhanced lesion**	
	Round, oval, linear, lobular	0
	Branching, spiculated, stellate	1
2	**Margin of contrast-enhanced lesion**	
	Well-defined	0
	Indistinca/ill-defined	1
3	**Enhancing pattern of the lesion**	
	Homogenous, non-enhancing internal septations	0
	In-homogenous	1
	Ring enhancement	2
4	**Initial signal intensity increase**[a]	
	Less than 50%	0
	50% to 100%	1
	More than 100%	2
5	**Signal intensity at 3-6 minutes after contrast injection**	
	Steady increase or continuous[b]	0
	Plateau[c]	1
	Washout[d]	2

[a] Initial peak signal intensity increase within the first 3 minutes after contrast material administration relative to the precontrast signal intensity. [b] Continued signal intensity increase=signal intensity increase of greater than 10% relative to the initial peak signal intensity at 3-8 minutes. [c] Plateau=deviation of the signal intensity at 3-8 minutes of (10%) relative to the initial peak signal intensity. [d] Washout=signal intensity decrease of greater than 10% relative to the initial peak signal intensity at 3-8 minutes.

Evaluation of enhancement kinetics following contrast agent administration was done on the post-processed dynamic images using the software function tool 2.6.4b3 of GE to measure the signal enhancement ratio within the lesions and identify the enhancement curves. Since accurate placement of a region of interest over the areas of most rapid and intense enhancement is critical we used color mapping of the lesions as a guide. We followed the quantitative method described by Fischer et al[1] to study the enhancement curves.

Evaluating the enhancement curves based on Fischer's group

The evaluation criterion was the peak percentage of signal intensity increase within the first 3 minutes after contrast material administration relative to the precontrast signal intensity (initial signal intensity increase). The initial signal intensity increase within 3 minutes was given a value of less than 50%, 50% to 100% and more than 100%. Furthermore, we evaluated the behavior of the signal intensity curve from the 3rd to the 7th minute. A signal intensity increase of more than 10% within this interval relative to the peak enhancement in the first 3 minutes was defined as "continued signal intensity increase" (giving a type I curve). A signal intensity similar to the peak signal intensity was considered as a plateau (giving a type II curve), and a decrease of more than 10% was defined as a washout (giving a type III curve).

The Fischer scoring system

In this scoring system, five dynamic contrast-enhanced MR features are evaluated. These comprised three morphological (shape, margins, enhancement kinetic) and two functional features (initial peak of signal intensity increase and behaviour of signal intensity curve) constituting a multifactorial protocol in which each criterion receives a point value. Each parameter is assigned points ranging from 0 to 1 or 0 to 2, with higher points for those that are more likely to be associated with malignancy. The sum of all the points defines the degree of suspicion of malignancy, with a score 0 representing the lowest and 8 the highest degree of suspicion (Table 1). The points are then assigned a BI-RAD category); 0 and 1 point correspond to category I (negative, no abnormal enhancement, enhancing masses or architectural distortion, 2 points corresponds to category II (benign findings, for routine follow up), 3 points correspond to category III (probably benign requires short interval follow up after 6 months), 4 and 5 points corresponds to category IV (suspicious abnormality, biopsy should be considered) and 6, 7 and 8 points correspond to category V (highly suggestive of malignancy, biopsy mandatory) . The appropriate points for each lesion were thus given to each feature and were recorded in the evaluation score table (Table 1). The BI-RADS category for the lesion was then identified (Figures 1-3). Tissue sampling was performed for cases with BI-RADS categories III, VI and V.

For the sampled lesions, the BI-RADS category was then compared with the tissue sampling result (by FNAC, core biopsy or lumpectomy/ mastectomy histopathology of the tumor). For non-sampled lesions, the BI-RADS category was determined by clinical follow up and repetition of MRI, ultrasonography (US) and/or mammography imaging at 12 and 24 months of the initial MRI scan. We then evaluated the accuracy of BI-RADS category using the Fischer scoring system for both benign and malignant lesions.

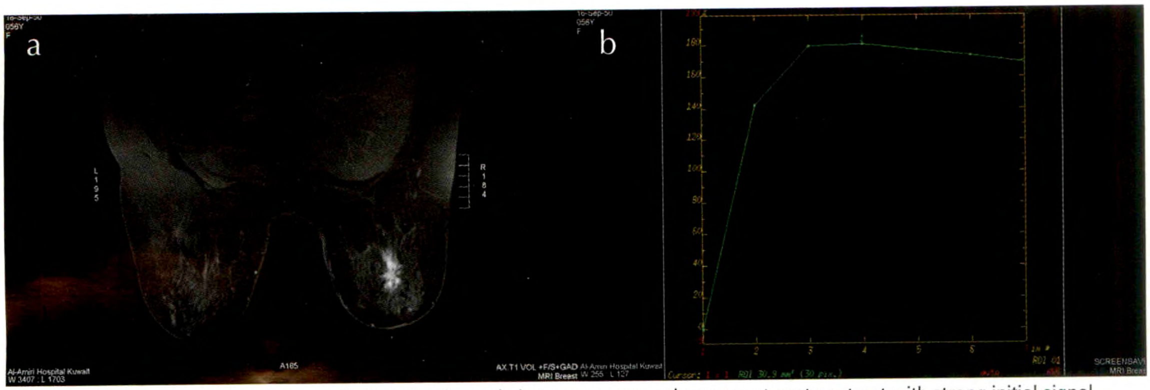

Figure 1. Left breast spiculated mass with ill-defined margin heterogeneous enhancement post contrast with strong initial signal increase and post-initial plateau (type II curve): a) post contrast fat saturated axial T1W image; b) enhancement curve (plateau). Spiculated mass (1 point), ill-defined margin (1 point), heterogeneous enhancement post contrast (1 point), strong initial signal increase (2 points) and post-initial washout (1 point): score 6 points, i.e. MRM BI-RADS category V. Proved ductal carcinoma postoperatively.

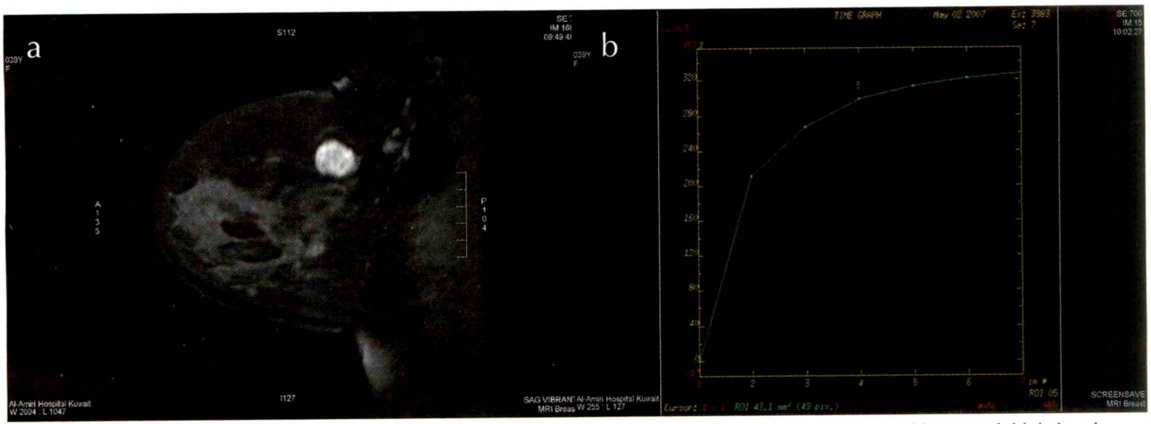

Figure 2. Left breast rounded mass with well-defined margin showing non-enhancing internal septations with strong initial signal increase, and continued signal intensity increase (type 1 curve): a) one minute post contrast fat saturated sagittal image; b) enhancement curve. rounded mass (0 point) , well-defined margin (0 point) , non-enhancing internal septations (0 point), strong initial signal increase (2 points), continued signal intensity increase (0 point): score 2 points, i.e. MRM BI-RADS category 2. Biopsy proven fibroadenoma.

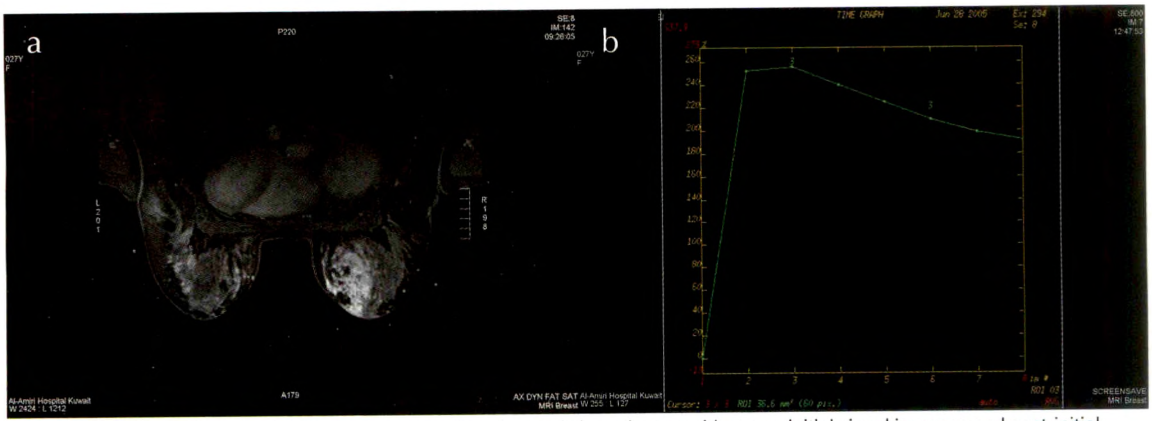

Figure 3. Right breast ill-defined, heterogeneously enhancing oval shaped mass with strong initial signal increase and post-initial washout (type III curve): a) post contrast fat saturated T1W image , b)enhancement curve (washout). Ill-defined mass (1 point), heterogeneously enhancing (1 point), oval shaped mass (0 point), strong initial signal increase (2 points), post-initial washout (3 points): score 7 points, i.e. the MRM BI-RADS category is 5. Histopathology proven chronic granulamatous mastitis.

RESULTS

Forty-one patients with identified breast lesions on mammography and ultrasonography were scanned with MRI using the 3D dynamic MRI protocol during May 2005 to September 2006. The age range of patients was 25 to 64 years with a mean age of 44.5 years and a median age of 44 years.

The total number of lesions identified in the 41 patients was 70. Seven of the 70 lesions were seen only on MRI and hence were not proven by tissue sampling since we had not yet started MRI-guided breast biopsy at that time and these were excluded from our study. Of the 63 lesions included in the study, 55 lesions were proved by tissue sampling. Twenty-five of the lesions were malignant and 30 were proven to be benign. Eight of the 63 lesions diagnosed by MRI as benign were not biopsied and were followed-up clinically and radiologically at 12 and 24 months after the initial MRI.

The histopathology of the 25 malignant lesions were well differentiated ductal carcinoma in situ in 5, poorly differentiated infiltrating ductal carcinomas in 8, well-differentiated invasive ductal carcinoma in 6, well-differentiated infiltrating lobular carcinomas in 5, and one well-differentiated mucinous carcinoma. Of the total breast lesions studied, the diagnostic yield of MRI was accurate in detecting malignant lesions in 92% and of benign lesions in 70%. Using the final histopathological diagnosis of the lesions as the gold standard , the sensitivity, specificity, positive and negative predictive values of MRI in diagnosing malignant breast lesions were 96%, 67%, 71% and 95%, respectively.

Morphological features of 25 pathologically proven malignant lesions

The margins were described as indistinct in 14 (56%) (Figure 1) and well circumscribed in 11 (44%). The shape was described as spiculated in 9 (36%) (Figure 1), round in 8 (32%) branching in 7 (28%) and lobular in 1 (4%). The enhancement pattern was homogeneous in 9 (36%), heterogeneous in 7 (28%) (Figure 1), peripheral rim in 8 (32%) and septated in 1 (4%). The mean size of the 25 carcinomas was 1.6 cm (range, 0.6 to 2.7 cm) for the homogeneously enhancing masses, 2.7 cm (range, 1.0 to 4.4 cm) for the heterogeneously enhancing masses, and 2.7 cm (range, 1.1 to 4.3 cm) for the rim-enhancing masses. Carcinomas less than or equal to 1 cm were significantly more common in the homogeneously enhancing group than in the heterogeneously or rim enhancing groups. Of the 25 carcinomas, 10 (40%) were less than 1 cm.

Morphological features of 30 pathologically proven benign lesions

The margins were described as well circumscribed in 25 (83%) (Figure 2) and indistinct in 5 (17%) masses. The shape was described as round in 14 (47%), branching in 8 (27%), linear in 4 (13%) and spiculated in 1 (3%). The enhancement pattern was homogeneous in 16

Table 2. The morphological features and kinetics of the proved benign lesions with BI-RADS IV and V categories.

	Category	Form	Margin	Enhancing pattern	Initial signal increase	Post-initial course
Lesion 1 Complicated cyst	BI-RADS IV	Branching			Strong	Plateau
Lesion 2 Benign	BI-RADS IV	Branching		Inhomogeneous	Strong	
Lesion 3 Chronic inflammation	BI-RADS IV		Indistinct	Inhomogeneous	Strong	
Lesion 4 Benign	BI-RADS IV		Indistinct	Inhomogeneous	Strong	
Lesion 5 Organizing inflammation	BI-RADS IV	Branching		Inhomogeneous	Strong	Plateau
Lesion 6 Scar tissue	BI-RADS IV				Strong	Washout
Lesion 7 Chronic inflammation	BI-RADS V	Spiculated	Indistinct	Inhomogeneous	Strong	Plateau
Lesion 8 Granulamatous inflammation	BI-RADS V	Branching	Indistinct	Inhomogeneous	Strong	Washout
Lesion 9 Granulamatous inflammation	BI-RADS V	Branching	Indistinct	Inhomogeneous	Strong	Washout

(53%), heterogeneous in 8 (27%), and with nonenhancing internal septations in 4 (13%) (Figure 2). The benign lesions that showed irregular or spiculated margin, branching and heterogeneous enhancement were proven to be chronic inflammation (Figure 3). The mean size was 2.2 cm (range, 0.5 to 4.0 cm) for the homogeneously enhancing masses, 3.2 cm (range, 0.3 to 6.0 cm) for the heterogeneously enhancing masses and 1.8 cm for the septated masses (range, 1.2 to 2.4 cm).

BI-RADS category of both benign and malignant lesions

The BI-RADS classification of the studied 63 lesions was as follows: 19 lesions were classified as BI-RADS V, 13 lesions as BI-RADS IV, 5 lesions as BI-RADS III, 14 lesions as BI-RADS II and 12 lesions as BI-RADS I. Among the 19 lesions classified as BI-RADS V, tissue sampling proved the lesions to be malignant in 16 masses and chronic inflammation in 3 lesions. Among the 13 lesions classified as BI-RADS IV, the lesions were proven by tissue sampling as malignant in 7 lesions, chronic inflammation in 3, complicated cyst in 1 and benign scar tissue in 2. Among the 5 lesions classified as BI-RADS III, 2 lesions were proven malignant and 3 lesions as benign by tissue sampling. Among the 14 lesions classified as BI-RADS II, 10 lesions were proven to be benign by tissue sampling and 4 lesions were proven benign by 2 years clinical and radiological follow up. Among the 12 lesions classified as BI-RADS I, 8 lesions were proven benign by tissue sampling and 4 lesions were proven benign by 2 years clinical and radiological follow-up. Eight lesions were not sampled since we did not started MR-guided breast biopsy at the time of the study. For the benign BI-RADS categories (I and II), the impression on MR mammography was consistent with the final diagnosis of a benign lesions in 100% of the cases. For the malignant MRM BI-RADS category (V), this was found to be consistent with the final diagnosis of malignancy in 84% of the lesions and of MRM BI-RADS category (IV) in 54% of the lesions. Thirty percent (9 out of 30) of benign lesions were diagnosed as malignant or probably malignant. No benign lesion was said to be of a category above II although in one case diagnosed morphologically as fibroadenoma and having BIRADS category III, the final diagnosis was invasive ductal carcinoma. The MRM BI-RADS category was consistent with the histological diagnosis of the 25 malignant lesions in 92% and of the 30 benign lesions in 70% of the masses. The overlapping features of chronic inflammatory lesions with carcinomas (Table 2, Figure 3) was the reason that the MRM BI-RADS category was of lower accuracy in diagnosing the benign lesions as compared to the malignant lesions.

DISCUSSION

In our study, we found that the Fischer scoring system[1] and the BI-RADS categories worked well for findings seen on MR imaging. For the 25 malignant lesions, only 2 masses were described as probably benign (BI-RADS category III). Of these one mass showed homogeneous enhancement and the other mass showed heterogeneous enhancement. Both showed circumscribed margins; one was round and the other was lobular in shape. The sizes of both masses were small (10 mm and 20 mm). All the descriptors used in these 2 cases are associated with a benign finding (category II) or probably benign finding (category III) in the final assessment categories. The reason behind this could be due to multiple factors, including limited spatial resolution of the dynamic sequences used and the overlap of enhancement, both in terms of kinetic measurements and morphologic appearances of benign and malignant lesions, which precluded complete differentiation of lesions.[8-11] If these small masses had not been biopsied, a 6-month follow-up would have been performed. As with mammography, if a change were noted at that time, biopsy was performed.

It is becoming increasingly clear that while most investigators have used either enhancement kinetics or lesion morphology in an attempt to differentiate benign enhancing lesions from enhancing breast cancer, an integrated interpretation strategy where enhancement kinetics data and morphologic feature analysis are used together for image interpretation may be superior to the use of either method alone.[12] Further, since reader variability remains a concern, an imaging lexicon similar to the BI-RADS lexicon used in conventional x-rays mammography, in which the architectural features are defined and illustrated, is needed.

To characterize a lesion as benign or malignant, one should integrate the morphological and the dynamic features of a lesion. The way to do it varies according to the experience of the investigator. For experienced radiologists, the classification of lesions can be done without the need of the scoring system suggested by Fischer et al.[1] In this case the classification of the lesion is done based on obvious features, e.g. BI-RADS V will be given to a stellate shape or spiculated border irrespective of the enhancement kinetics[13,14] and for other lesions with irregular shape and non-smooth borders and heterogeneous architecture the kinetics are referred to; if there is strong enhancement and washout it is classified as BI-RADS V and if intermediate enhancement with plateau or persistent time course it will then be classified as BI-RADS IV. Classifying a lesion using this method works very well for experienced radiologists, but for inexperienced radiologists this might be confusing and might cause over- or underestimation of the BI-RADS category of a lesion.

Evaluating the enhancement curves can be done with either a qualitative[11] or quantitative method.[1] Kuhl et al[8] described three types of time-intensity curves: type I (steady enhancement), where a persistent increase in signal intensity is present beyond 2 minutes after contrast agent injection; type II (plateau), where the maximum signal intensity is achieved in the first 2 minutes and then remains fairly constant; and type III (washout), where the maximum signal intensity is achieved in the first 2 minutes and then decreases over time. It has been reported that the type I curve is usually seen in benign lesions and normal breast parenchyma, the type III curve is mostly seen in malignant lesions and some fibroadenomas and the type II curve is equivocal and seen in some benign lesions and many malignant lesions.[8] The qualitative method needs experience and is prone to under or overestimating the curve pattern especially in deciding whether it is a plateau (type II curve) or a wash-out (type III curve) pattern. The quantitative method, however, is easier and gives the inexperienced reader more confidence in characterizing the enhancement curve of a lesion.

Non-enhancing internal septations, a descriptor usually associated with fibroadenomas, is a sign that is no longer exclusive to benign lesions since recent results of a study by Schnall et al[11] revealed that 47% of malignant lesions were shown to have nonenhancing internal septa. In our study, one septated mass that was detected and given BI-RADS III category proved to be well differentiated invasive ductal carcinoma. None of the 25 carcinomas was assigned a final assessment of category I or II. Also, most of them were assigned a BI-RADS category IV (28%) or category V (64%), necessitating biopsy even by those radiologists who had no experience interpreting breast MR images.

For the 30 benign lesions the overall accuracy was less (70%). Three lesions were scored as BI-RADS V and 6 lesions as BI-RADS IV. Looking at the pathological diagnosis, morphology and the kinetics of these lesions (Table 2), we found that 5 of these lesions were chronic inflammatory lesions and 1 mass was scar tissue. The morphologic features of these inflammatory lesions were overlapping with those of the malignant lesions (Figure 3). The difficulty in accurately differentiating chronic inflammation from invasive carcinoma was also reported by Rieber et al.[15] The inclusion of chronic inflammatory lesions in our study is the main reason for a reduced accuracy since MRI is not a good tool for the differentiation of benign from malignancy in such a clinical situation.

In our study, we noticed a higher prevalence of homogenous enhancement than heterogeneous and rim enhancement in malignant lesions. We also noticed that the mean size of carcinomas showing homogeneous enhancement was smaller than the mean size of carcinomas showing rim or heterogeneous enhancement. The reason behind this could be that 40% of the carcinomas in the current series were less than 1 cm in size. Rim enhancement, seen in 33% of the ductal carcinomas and in 60% of the lobular carcinomas in this series, is considered a suspicious morphologic feature.[2] The case of mucinous carcinoma in this series did not exhibit rim enhancement.

Nunes et al[5] found that none of the malignant masses had smooth borders, unlike our study in which 44% of the carcinomas had circumscribed borders. Nevertheless, most of these lesions had other more worrisome descriptors, such as heterogeneous or rim enhancement, which could be interpreted as malignancy as previously reported.[13] Moreover, mammographically circumscribed masses can be malignant, particularly the specific histologic subtypes of medullary, colloid, and papillary carcinoma as 5% to 6% of malignant masses have been described as circumscribed.[16]

In our study, we noted that there was a good correlation between the MRM-BI-RADS final assessment category and the eventual diagnosis obtained on histopathology or follow-up. One weakness of our study was that we were forced to exclude 7 lesions from the study and analysis as they required MR-guided biopsy that we did not perform at the start of the study. It is no doubt important to have the facility of performing biopsies under MR guidance for lesions not accessible by other modalities and in whom a wait and watch policy is not advised.

It is logical that mammographers who are accustomed to evaluating breast lesions using BI-RADS terms on mammography can readily translate those skills to MRI. The assignment of a final assessment category, as in mammography, indicates to the referring physician what appropriate step should be taken next and what information should be included in the report.

In conclusion, the MRM BI-RADS lexicon using the Fischer system is easy to apply and very useful and accurate in characterizing breast lesions. Overlapping MR features between some benign lesions like chronic inflammation and malignancy that might reduce the specificity need to be interpreted in conjunction with the clinical presentation and all other pertinent breast imaging studies, such as mammography and ultrasonography.

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original article

Clinicopathological study of male breast carcinoma: 24 years of experience

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Ann Saudi Med 2009; 29(4): 288-293

BACKGROUND AND OBJECTIVES: Because breast cancer in men is rare, few patients are available for prospective studies. To learn more about its epidemiology, risk factors, clinical features, genetics and pathology in our country, we conducted a retrospective study of all cases seen in recent decades at our institution.
PATIENTS AND METHODS: We identified each case of male breast cancer in the database at the Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir, India, between the years 1983 to 2007.
RESULTS: We identified only 32 cases of male breast cancer over the 24-year period. Male breast cancer accounted for 32 (2.8%) of 1141 resected breast specimens, which included all breast lesions and 32 (4.1%) of 780 breast cancer cases. Of the 32 cases, 20 (62.5%) had various associated risk factors. Invasive ductal carcinoma was seen in 30 cases (93.7%). Of 20 cases that underwent molecular studies, 16 (80%) patients had estrogen receptor positivity whereas 14 (70%) had progesterone receptor positivity. Six cases (30%) overexpressed HER2 and p53. The *BRCA2* mutation was observed in 4 cases (40%) while no patient presented with the *BRCA1* mutation.
CONCLUSION: An incidence of 4.1% for male breast cancer indicates that this disease is not as uncommon as presumed in this part of the world. Breast cancer in men seems more frequently to be hormone receptor positive and the *BRCA2* mutation confers a significant risk to men.

Breast cancer in males is relatively uncommon, accounting for less than 1% of all breast cancers and less than 1.5% of all malignancies in men.[1-3] With the exception of Tanzania and countries of central Africa, male breast cancer is distributed uniformly throughout the world.[4,5] The incidence of male breast cancer has remained stable over the past four decades. Because of this low incidence, unlike carcinoma of the breast in women, a limited number of patients are available for study. Even large oncological centers have relatively small numbers. It comes as a shock to many to learn that men too can get breast cancer.[6] In the present study, we review our experience of 24 years with this disease, focusing on its epidemiology, risk factors, genetics, pathology and molecular markers.

PATIENTS AND METHODS

For this retrospective study, we identified all male breast cancer patients seen from January 1983 to December 2007 at the Department of Pathology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir. The history, including tumor size, histological and nuclear grades, was evaluated. The TNM classification system was used for tumor staging. Histological material for study was available in all cases. Data on epidemiology, risk factors, clinical assessment, genetics, pathology and molecular markers were the focus of study.

Immunohistochemical studies were done routinely in breast carcinoma cases seen in the last decade. In some cases reported earlier, immunohistochemistry was done as part of the present study. Molecular marker studies were done in 20 cases and genetic studies in 10 cases. For immunohistochemical studies, 5-µm sections of formalin-fixed, paraffin-embedded tissue were cut and placed on gelatin-coated slides. Estrogen receptor, progesterone receptor and p53 immunostaining were performed using the avidin-biotin complex peroxidase technique with the chromogem diaminobenzidine and with the microwave antigen retrieval technique. ER and PR nuclear stains were categorized as positive or negative. Positive staining was established as >50% of the cells showing distinctive nuclear stain; p53 immunoreactivity was interpreted using the criteria described by Thor and Yandell.[7] The tumor was scored positive if cells showed strong uniform staining of the nuclei; as intermediate for weak or focal nuclear staining and as negative for no staining. ER, PR, p53 and HER2 protein, immunohistochemical studies were performed in 20 patients (62.5%) whereas 10 patients (31.2%) had *BRCA1* and *BRCA2* detection. Immunohistochemistry was the only method used for detection of *BRCA1* and *BRCA2* mutations. In 10 cases (31.2%) of male breast carcinoma, formalin-fixed, paraffin-embedded blocks were analyzed using monoclonal antibody for the *BRCA1* protein (anti-*BRCA1* [Ab-1], human [mouse]: epitope: 1-304 N-terminal aminoacids of BRCA1) and a polyclonal antibody for the *BRCA2* protein (anti-*BRCA2* [Ab-2], rabbit polyclonal Ig G: epitope: 3245-3418 of human *BRCA2*) (Oncogene Research Products/Calbiochem, Darmstadt, Germany) at a dilution of 1:300 and 1:100, respectively. Antigen retrieval was performed by heating the specimens in a pressure cooker for 6 minutes in citrate buffer (pH 6). The Envision system (Dako, Copenhagen, Denmark) was used for detection. Sections from positive breast invasive ductal carcinoma were used as positive controls, and negative controls were obtained by omitting the primary antibodies. The reaction was considered positive if more than 10% of the cells showed distinctive nuclear staining.[8] HER2-protein expression was carried out by the immunohistochemistry method using monoclonal antibody (CB 11-NOVOC-Castra, Newcastle upon Tyne, UK) (TAB 250, Zymed, San Francisco CA, USA). The test was carried out on tumor tissue samples fixed in buffered formalin and embedded in paraffin wax. Based on an assessment of the intensity of the reaction product and percentage of positive cells, scoring of *HER2* expression was graded from 0 to 3+.[9]

Table 1. Risk factors for male breast carcinoma.

Testicular abnormalities	
Undescended testis	3
Congenital inguinal hernia	Nil
Orchidectomy	Nil
Orchitis	2
Testicular injury	Nil
Infertility	3
Klinefelters syndrome	Nil
Positive family history	1
Obesity	4
Radiation exposure	1
Other factors	Nil
Breast cysts	4
Breast trauma	1
Gynecomastia	10

RESULTS

The incidence of carcinoma of the male breast was 2.8% (32/1141) of the total resected breast specimens, which included all breast lesions and 4.1% (32/780) of total breast cancer cases. Mean age at presentation was 55 years (range, 40 to 70 years), with the youngest patient being 40 years old and the oldest 70 years old. Of the 32 cases in this study, 20 cases (62.5%) had various risk factors for male breast carcinoma (Table 1). Testicular abnormalities with infertility were seen together in 3 cases (9.3%). One case had a history of radiation exposure and one had a positive family history and obesity. Sixteen (50%) patients had a painless breast mass (Table 2). Nipple and skin retraction was seen in 12 patients (37.5%). A retroaerolar presentation was the most common site. Twenty-two patients (69%) presented with nodal positivity. Twelve cases (37.5%) had 1-3 lymph nodes positive whereas 10 cases (31.2%) had more than 4 lymph nodes positive. In 10 cases (31.2%)—lymph nodes were free of tumor. Eighteen patients (56.2%) presented with stage III disease, but a significant number—12 (37.5%) and 10 (31.2%)-presented with stage II and stage I disease, respectively. No patient had stage IV carcinoma. Fine needle aspiration cytology smears and conventional pathologic features were evaluated. Cytology of aspirate smears revealed malignancy in 30 cases (93.7%). Material was inadequate in 2 cases (6.2%). Most of our cases (30 cases, 93.7%) were invasive ductal carcinoma, with one each (3.1%) of papillotubular carcinoma and adenoid cystic carcinoma (Table 3). In our series we saw no patient with Paget disease of the nipple. The various genetic and molecular markers are summarized in Table 4.

DISCUSSION

The phenotypic alterations of male breast tumor are not well studied, and experience is mainly inferred from that of female breast cancer. Although both diseases have similarities, there are notable differences in risk factors, prognosis and survival. Differences between male and female breast carcinoma have been noted;

Table 2. Clinical features in 32 cases of carcinoma of the male breast.

Clinical Features	Invasive (n=28)	Non-invasive (n=4)
Mean age (years) (range)	55 (30-75)	56 (50-60)
Mean duration of symptoms (months) (range)	3 (1 month-1 year)	9 (6 months-1 year)
Mass	16/32 (50%)	4/32 (12.5%)
Mean size (cm) (range)	2 (0.5-4.5)	1.0 (1.0-2.0)
Site		
Retroaerolar	24/32 (75%)	4/32 (12.5%)
Upper outer quadrant	8/32 (25%)	-
Skin and nipple retraction	12/32 (37.5%)	-
Lymph node metastasis	22/28 (78%)	0

Table 3. Histopathological tumor type.

Invasive ductal carcinoma	30 (93.7%)
Papillotubular carcinoma	1 (3.1%)
Solid tubular	Nil
Schirrhous carcinoma	Nil
Lobular carcinoma	Nil
Adenoid cystic carcinoma	1 (3.1 %)
Paget's disease	Nil
Total number of cases	**32**

Table 4. Pathologic and genetic features of breast carcinoma in men.

Pathological Features	Total number of cases	Number of cases positive or immuno-reactive	
Estrogen receptor	20	16	80%
Progesterone receptor	20	14	70%
HER2	20	6	30%
p53 protein	20	6	30%
BRCA1	10	Nil	Nil
BRCA2	10	4	40%

male breast carcinoma has a tendency to present at higher clinical stages and with more lymph node metastases. The incidence of breast cancer in males, unlike that in females, has not increased appreciably over the last 40 years.[3] The incidence increases exponentially with age.[10] In most western countries, men account for approximately 1% of cases of breast carcinoma. In Tanzania, by contrast, 6% of cases of breast cancer are diagnosed in men,[4] and in countries of central Africa, a substantially higher proportion of cases of male breast cancer have been reported.[5] The reasons for this geographic variability remain unclear. However, this may be due to a higher prevalence of liver disease (schistosomiasis or malnutrition), resulting in an increase in endogenous estrogens. In a study conducted at a tertiary care hospital in the eastern part of India, the reported incidence of male breast cancer was 0.6% among all male cancers and 2.5% among all breast cancer cases.[11] In recently published data from a neighboring country (Pakistan), male breast cancer constituted 4.6% of all breast carcinomas.[12] We report an incidence of 4.1% of the total breast cancer cases, which is higher than the generally reported incidence of 1% worldwide. This higher incidence is possibly due to our institute being a referral center. Many of the risk factors for breast cancer in men, as in women, may be hormonally driven. An elevated risk has been seen in patients with undescended testes, congenital inguinal hernia, orchidectomy, orchitis, testicular injury and infertility.[4,5,11,13] In our study, there were 3 cases (9.3%) each of undescended testes and infertility. Orchitis was reported in 2 cases (6.2%). Other possible risk factors that relate to hormonal levels include obesity, which increases peripheral aromatization of estrogen, and cirrhosis, which results in a hyperestrogenic state.[14,15] Estrogen has a profound effect on male breast tissue and is able to stimulate formation of acini and true lobules identical to those of the female breast. There have been many reports of breast tumors developing in men undergoing estrogen therapy for prostrate carcinoma that have proved to represent secondary involvement of an estrogen-altered breast as part of the metastatic process. Alterations of hormonal metabolism in men with breast cancer have been demonstrated, but no consistent pattern has emerged. Several studies have implied an association between testicular abnormalities and male breast cancer. Prior orchitis has been reported more frequently among men with breast cancer than among controls. Obesity, especially that occurring before the age of 30 years, may be another risk factor. The presumed mechanism is increased conversion of androgens to estrogens through peripheral aromatization. Four (12.5%) of our patients were obese and 10 (31.2%) patients had gynecomastia. A rare malignancy, male breast cancer has in epidemiological studies been associated with a prior history of gynecomastia.[16,17] However, a recently conducted prospective study in men with gynecomastia confirmed an increased risk for testicular, skin and esophageal cancers whereas no prospective cases of male breast cancer were seen.[18] It was concluded that before gynecomastia is included as a risk factor for male breast cancer, a man presenting with gynecomastia should be evaluated for the following: Is there a endogenous or exogenous hormonal cause? Has the patient been taking drugs that may cause gynecomastia? Is there a known accompanying disease causing a liver or gonadal injury? Can tumor disease in the testis, skin and breast be excluded on clinical grounds?

There are a few studies that have addressed meat consumption and the risk of male breast cancer.[19,20] Conflicting reports have emerged, but in our study all 32 patients were red meat eaters. Although meat as a risk factor for getting male breast cancer has not been studied in a study from the same geographical region (Pakistan) showed an identical incidence of male breast carcinoma.[12] It would be interesting to study meat consumption as an epidemiological risk factor, since most of the population in Kashmir and Pakistan consume red meat in large quantities.

Approximately 15% to 20% of male patients with breast cancer have a positive family history, although only 7% of the general male population has an affected family member.[21,22] Therefore, researchers have suspected that some families may carry genetic mutations that provide an increased risk for breast cancer. In our series, one patient had a positive family history. This patient had a first-degree relative with breast cancer. In men, *BRCA1* does not appear to be associated with a significantly increased risk for breast cancer, although mutations in this gene have been described in affected men.[23] However, men with *BRCA2* mutations are predisposed to breast cancer. This gene was first identified by Wooster who localized it to chromosome 13q12-13 and described multiple cases of breast cancer in men that showed linkage to this area.[24] Families in which breast cancer has occurred and where at least one male has been affected have been reported to have a 60% to 76% chance of carrying *BRCA2* mutations.[25] Thus, the presence of breast cancer in men within a family with documented breast cancer indicates a high likelihood of a *BRCA2* mutation. In 10 patients (31.2%) tested for genetic mutations *BRCA1* and *BRCA2*, *BRCA2* positively was seen in 4 cases (40%). No immunoreactivity was seen with *BRCA1*. One case (10%) of male breast carcinoma with a positive family history had *BRCA2* mutation positivity. Eleven percent to 40% of men with breast cancer carry this mutation.[26] The highest known prevalence of *BRCA2* mutations in male patients with breast cancer is in Iceland, where a founder mutation accounts for 40% of all cases.[27] Little is known about the distinguishing characteristics of breast cancer in men with *BRCA2* mutations, although men with a mutation may present with disease at an earlier age.[28]

Almost all of the histologic subtypes of breast carcinoma that have been diagnosed in women have also been reported in men. Approximately 90% of all breast tumors in men are invasive carcinomas, the remaining 10% are non-invasive. In our study, 30 cases (93.7%) were invasive carcinomas and the remaining were noninvasive. The proportion of noninvasive cancers is higher than that seen in women before the introduction of mammography and may be due to the small size of the male breast, which simplifies the detection of small breast masses.[29] Almost all of the noninvasive cancers are ductal carcinomas in situ. Lobular carcinoma in situ is extremely rare because of the absence of terminal lobules in the normal male breast.[21] Ductal carcinomas in situ of the male breast differ from that of the female breast in that 75% of cases are a papillary subtype and almost all cases are low to intermediate grade.[30]

In men, the predominant histologic subtypes of invasive carcinoma are infiltrating ductal carcinoma, which accounts for more than 80% of all tumors, and papillary carcinoma, which makes up about 5%.[31] Lobular carcinoma is much less common in men than in women and represents only 1% of all cases.[21] The rare subtypes, such as medullary, tubular, mucinous and squamous carcinomas, have all been reported in men,[31] although they are slightly more uncommon than in women. Inflammatory carcinoma and Paget disease are seen with a similar frequency in men and women.[29]

Carcinomas of male breast have a higher rate of hormone receptor positivity than do carcinomas of the female breast when matched for tumor stage, grade and patient age.[32] Our study indicates that 80% of male breast carcinomas are estrogen-receptor positive and 70% are progesterone receptor positive. This is in conformity with other studies.[21,33]

However, hormone expression up to 95% has been shown in a study by Wang-Rodriguez et al.[34] Aberrant steroid receptor up-regulation as a consequence of constitutive activation of downstream targets in the estrogen-starved postmenopausal setting and in male breast patients have been postulated for hormone receptor expression.[35]

HER2, p53, bcl-2, cyclin D1 and epidermal growth factor (EGFR) are important in the pathogenesis and prognosis of breast cancer in women. In our data (Table 4), only in 20 cases (62.5%) were p53 and HER2 available. The *HER2* protooncogene encodes a membrane of the EGFR family, and is located on chromosome 17q21. This receptor is expressed in 20% to 30% of breast cancers in females and its positivity is related to high grade tumors, lymph node metastasis, a higher rate of disease recurrence, higher mortality and thus a poor prognosis. Further *HER2* status is a predictive factor of response to particular systemic therapies, notably trastuzumab. The College of American Pathologists (CAP) both consider *HER2* testing to be part of the standard workup for a newly diagnosed breast cancer.[36,37]

P53, a tumor suppressor gene, controls cell growth by including cell-cycle blockade, apoptosis and cell differentiation. A positive test for mutation indicates a poor prognosis. A review of literature revealed that between 18% and 58% of male breast cancers test positive for *P53* by immunohistochemistry,[38,39] which is confirmed by our results. Though carcinoma of male breast has a similarity to its female counterpart, it differs genetically. *BRCA1* and *BRCA2* can cause breast cancer in females, but only *BRCA2* mutation confers a significant risk to men. Of 32 cases of male breast carcinoma in our series, a genetic marker study was available in 10 cases (31.2%). Of these cases, 4 (40 %) cases were immunoreactive the *BRCA2* mutations and were also positive for estrogen and progesterone receptors. Among these four cases was one case with a documented family history of breast carcinoma. Higher rates of estrogen and progesterone receptor positivity may be observed in men than in women, but similar percentages may be expressed for *HER2* and p53. Larger studies for pathological markers will certainly reveal genetic abnormalities that play a role in the pathogenesis and also ascertain various prognostic markers. The cell surface glycoprotein E-cadherin (CDH1) is a key regulator of adhesive properties in epithelial cells. Germline mutations in CDH1 are well established as the defects underlying heredity diffuse gastric cancer (HDGC) syndrome along with an increased risk of lobular breast cancer (LBC) have been described in HGDC kindreds. Pleomorphic lobular carcinoma shares some characteristics with classic infiltrating lobular cancer, although it may also have distinctive features, thus raising the question of whether pleomorphic lobular carcinoma is a tumor of a lobular nature. In this context, several studies have demonstrated that the analysis of E-cadherin expression is a powerful tool for distinguishing lobular from ductal carcinomas, even in those infiltrating and in situ tumors with indeterminate features.[40,41] Consistent with these findings, E-cadherin gene (CDH1) has been reported to be frequently mutated in infiltrating lobular carcinoma[42-44] and lobular carcinoma in situ,[45] but not in ductal tumors.[46]

An incidence of 4.1% of male breast cancer indicates that this disease is not that uncommon as presumed in this part of the world. The population of patients with various risk factors must be evaluated for such lesions. Breast cancer in men seems more frequently to be hormone-receptor positive and the *BRCA2* mutation confers a significant risk to men. Areas for future investigations are many and larger studies of pathological markers would be helpful to define which genetic abnormalities play a role in breast cancer in men and to determine which markers are important prognostic factors. It is further stressed that major epidemiological studies in populations at higher risk are needed to explore the various etiological factors.

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A screening tool for attention deficit hyperactivity disorder in children in Saudi Arabia

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Ann Saudi Med 2009; 29(4): 294-298

BACKGROUND AND OBJECTIVES: A clinically validated attention deficit hyperactivity disorder (ADHD) scale in Arabic for evaluating children in Saudi Arabia who might be suspected of having ADHD is lacking. Thus, we studied the validity of an Arabic version of the ADHD Rating Scale in discriminating children with an ADHD diagnosis from normal children or from those with non-ADHD psychiatric diagnoses, including mental retardation.

METHODS: The guardians of 119 children provided demographic data and completed the standardized Arabic version of the ADHD Rating Scale on their children, who were either normal, had a diagnosis of ADHD, or had a non-ADHD psychiatric diagnosis. The mean rating scores of the groups were compared, and the cutoff points were calculated for both sexes.

RESULTS: The scores discriminated children with ADHD diagnosis (mean and [SD], 28 [6.288]) from normal children (10.93 [8.009]), and those with a non-ADHD psychiatric diagnosis (16.63 [8.865]). ADHD cutoff points were obtained for male (23.5) and female (22.5) children. Psychosocial characteristics associated with children having ADHD were not associated with the diagnosis of ADHD.

CONCLUSION: The ADHD Rating Scale (Arabic version), in terms of either the grand total score or the total score of each of its two subscales, demonstrated concurrent and discriminant validity by discriminating children with ADHD from other clinical and non-clinical children groups. The study obtained cutoff points for both sexes based only on the grand total score of the scale because of the relatively small sample size. Replication of the study, utilizing a larger sample and eliciting ratings from both parents and teachers, is recommended.

There is a general consensus that well standardized behavior rating scales are essential in the evaluation of children with attention deficit hyperactivity disorder (ADHD). However, such rating scales have their limitations. They are subject to biases in opinion, such that various characteristics of the informants, including their education and emotional state at the time of conducting the ratings, may influence the ratings. Also, rating scales may fail to assess factors influencing a child's behavior.[1] Other sources of limitation are inherent to the construction of the rating scales themselves, including the specificity of wording and the breadth of response scaling. In addition, demographic variables may produce situational variation in a child's behavior[1] or in the way children's parents, for example, may perceive and rate the behavior of their children.[2] There are several types of behavior rating scales that have been used in assessing ADHD symptoms in children and adolescents. However, there is no well-validated scale in Arabic for children. Our study aimed at validating children in Saudi Arabia one of the most commonly used scales, the ADHD Rating Scale[3] for use in screening children with ADHD symptoms. The scale was selected because of its established ability to discriminate ADHD children from those in clinical and normal populations,[1] and because it provides a direct rating of the essential symptoms of the disorder as per the diagnostic criteria of the Diagnostic and Statistical Manual (version 3, revised (DSM-III-R).[4] This study predominantly focused on examining the validity of the grand total score of the ADHD Rating Scale (Arabic Version) in discriminating children with ADHD from either normal children or children with any of a set of psychiatric diagnoses other than ADHD.

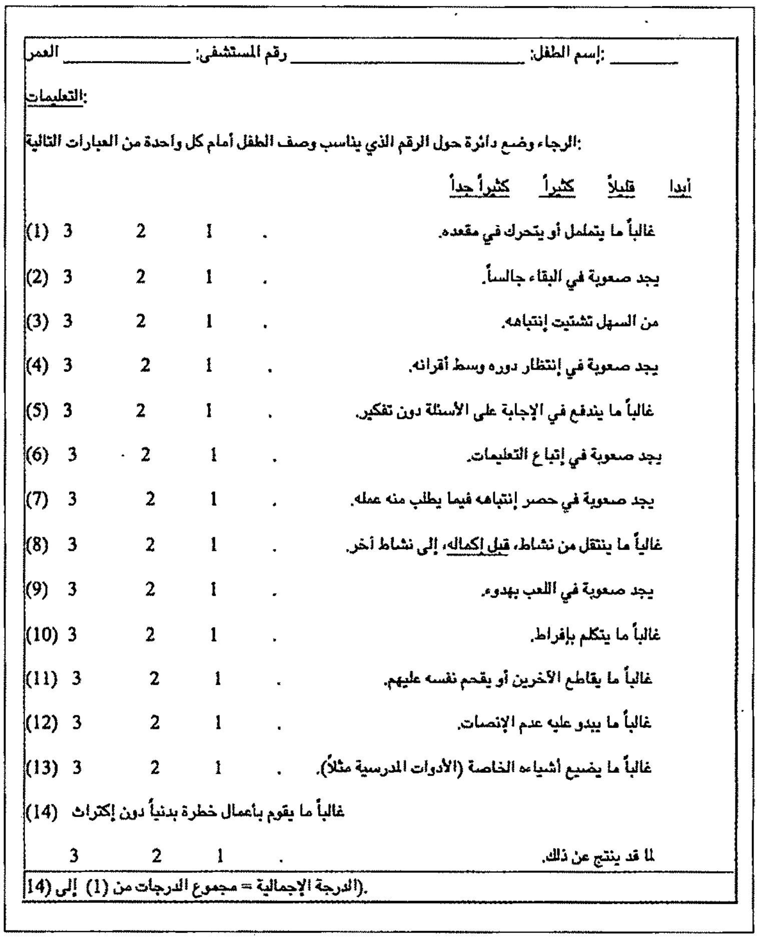
METHODS

The ADHD Rating Scale (Arabic version) (Figure 1) is the translated and linguistically standardized version of the original ADHD Rating Scale.[3] It contains 14 items, each of which is a 4-point scale (0-3) arranged in the following format: not at all, just a little, pretty much, very much. The scale, in its original language, has an established test-retest reliability and internal consistency reliability. In addition, it has established construct, discriminant, and concurrent validity measures. The completion time for the scale is 5 minutes. Finally, the administration of the scale can yield three scores: a) grand total score, b) inattention-restlessness sub-scale score (containing items that are intended to screen specifically the symptoms that are assumed to be pertinent to the factor of inattention/restlessness), and c) impulsivity-hyperactivity sub-scale score (containing items that are intended to screen specifically the symptoms that are assumed to be pertinent to the factor of impulsivity/hyperactivity).

The Department of Translation, King Saud University was consulted for the processes of translation and back-translation, while the technical adaptation of the scale was performed by the researchers who, after a pilot study (n=56), examined and adapted the Arabic version to ensure that it preserved the format, consistency and content of the English version of the scale. Personal and demographic data about the participants in the study, including information about the child, his or her parents, siblings, and the principal guardian if not one of the parents were collected. These include family structure and size, educational level of the child and his parent/guardian, status of parental marriage (i.e., living together or separated), the other socioeconomic data.

The ADHD Rating Scale[3] is based on the DSM-III-R construct of attention deficit hyperactivity disorder, since it was the current DSM edition at the time of publishing the rating scale. The researchers in this study found it appropriate to use the scale at the onset of the study in early 1995 by which time the 4th edition was published,[5] since there were no significant differences, as far as the ADHD construct was concerned, between the two editions. For example, the DSM-IV criteria require impairment across settings, while this study focused on both parent ratings and clinical assessment since access to the school setting was not attainable. However, while the DSM-III-R did not identify any subtypes of ADHD, the DSM-IV has conceptualized ADHD as consisting of three subtypes: Inattentive, Hyperactivity-Impulsivity, and Combined.[6]

In 1995, the original ADHD Rating Scale[3] was translated into Arabic and was pilot studied (n=56) by three psychiatrists and a clinical psychologist from three major mental health centers in Riyadh, Saudi Arabia (The Departments of Psychiatry in Riyadh Military Hospital and King Khalid University Hospital and Riyadh Mental Health Hospital). The main study subjects were freshly recruited on a first-come first-included basis at the child mental health clinics of the three participating mental health centers. The guardians of children participating in the study were interviewed to elicit their consent for participation in the study, and they completed the structured, purpose-built data collection form. The guardians of the children were then asked to rate their children using the standardized Arabic version of the ADHD Rating Scale. In two of the three centers, the clinician who confirmed the psychiatric diagnosis of the children was always different from the clinician who processed the completion of the data collection form with the guardian of the respective child and who handed the ADHD Rating Scale (Arabic version) to the respective child guardian to complete. The sub-sample of normal children was recruited from among the child population visiting the immunization clinic in one of the three mental health centers



إسم الطفل: ______ رقم المستشفى: ______ العمر ______

التعليمات:

الرجاء وضع دائرة حول الرقم الذي يناسب وصف الطفل أمام كل واحدة من العبارات التالية:

أبدا قليلاً كثيراً كثيراً جداً

(1) 3 2 1 . غالباً ما يتململ أو يتحرك في مقعده.
(2) 3 2 1 . يجد صعوبة في البقاء جالساً.
(3) 3 2 1 . من السهل تشتيت إنتباهه.
(4) 3 2 1 . يجد صعوبة في إنتظار دوره وسط أقرانه.
(5) 3 2 1 . غالباً ما يندفع في الإجابة على الأسئلة دون تفكير.
(6) 3 2 1 . يجد صعوبة في إتباع التعليمات.
(7) 3 2 1 . يجد صعوبة في حصر إنتباهه فيما يطلب منه عمله.
(8) 3 2 1 . غالياً ما ينتقل من نشاط، قبل إكماله، إلى نشاط أخر.
(9) 3 2 1 . يجد صعوبة في اللعب بهدوء.
(10) 3 2 1 . غالباً ما يتكلم بإفراط.
(11) 3 2 1 . غالباً ما يقاطع الآخرين أو يقحم نفسه عليهم.
(12) 3 2 1 . غالباً ما يبدو عليه عدم الإنصات.
(13) 3 2 1 . غالباً ما يضيع أشياءه الخاصة (الأدوات المدرسية مثلاً).
(14) غالباً ما يقوم بأعمال خطرة بدنياً دون إكتراث
3 2 1 . لما قد ينتج عن ذلك.

(الدرجة الإجمالية = مجموع الدرجات من (1) إلى (14)).

Figure 1. Attention deficit hyperactivity disorder rating scale (Arabic version).

Table 1. Sex distribution of the diagnostic groups.

Diagnostic group	Males (%)	Females (%)	Total (%)
Normal	15 (12.6)	14 (11.8)	29 (24.4)
ADHD diagnosis only	13 (10.9)	05 (04.2)	18 (15.1)
ADHD+ psychiatric diagnosis	11 (09.2)	02 (01.7)	13 (10.9)
Psychiatric diagnosis	34 (28.6)	12 (10.1)	46 (38.7)
Mental retardation	07 (05.9)	06 (05.0)	13 (10.9)
Total	80 (67.2)	39 (32.8)	119 (100)

Table 2. Multiple comparisons of diagnostic group mean grand total scores on the ADHD Rating Scale (Arabic Version).

	Normal	ADHD diagnosis only	ADHD+other psychiatric diagnosis	Psychiatric diagnosis
ADHD diagnosis only	a			
ADHD+ psychiatric diagnosis	a	0.998		
Psychiatric diagnosis	0.076	a	a	
Mental retardation	0.270	b	b	1.000

[a]*P*<.001; [b]*P*<.05 (Scheffé Test).

Table 3. Multiple comparisons of diagnostic group mean scores on the "Inattention-Restlessness" sub-scale of the ADHD Rating Scale (Arabic Version).

	Normal	ADHD diagnosis only	ADHD+other psychiatric diagnosis	Psychiatric diagnosis
ADHD diagnosis only	a			
ADHD+ psychiatric diagnosis	a	0.991		
Psychiatric diagnosis	0.610	a	a	
Mental retardation	0.910	b	b	1.000

[a]*P*<.001; [b]*P*<.01 (Scheffé Test).

participating in the study. The recruited children were subsequently screened by one of the psychiatrists.

This study sample included 119 children, of which 90 (89.1%) had various psychiatric diagnoses confirmed by a psychiatrist, and 29 (10.9%) were clinically screened by a psychiatrist to be normal children. The normal children as well as those with psychiatric diagnoses were subsequently designated to the following diagnostic groups: normal, ADHD diagnosis only (ADHD Dx), ADHD diagnosis combined with another psychiatric (Axis I) diagnosis (ADHD+Psy Dx), Psychiatric (Axis I) diagnosis only (Psy Dx) and mental retardation only (MR).

The data were tabulated and analyzed using the Statistical Package for Social Sciences, version 10 (SPSS 10). The chi-square test was used for categorical variables, the t test for numerical variables, and one-way analyses of variance (ANOVA) and Scheffé test for more than two-group analysis. For determining the cutoff points, including sensitivity and specificity measures, based on the grand total score of the scale, the receiver operating characteristics (ROC) curve was plotted.

RESULTS

The study included 119 children (80 males, 39 females) (Table 1) with a mean age of 8 years (range, 3 to 13 years). Of these 119 children, 112 (94.2%) were 5 years of age or older. Of the whole sample, 58 (48.7%) had no schooling, 55 (46.1%) were in primary education, and 4 (3.4%) had no information on their education. There were no significant differences between the groups in most demographic variables, but the diagnostic groups differed significantly (*P*=.0001) in terms of the children's years of formal schooling, with the children in the normal group having a higher mean school grade than that of the ADHD plus and the mental retardation groups.

Children in the ADHD diagnosis only and the ADHD plus psychiatric diagnosis groups had significantly higher grand total scores compared to children in the normal group (*P*<.001) or in either the mental retardation (*P*<.05) or the psychiatric diagnosis (*P*<.001) groups (Table 2). The mean (SD) scores for each diagnostic group were as follows: AHDH diagnosis 28.0 (6.288), normal 10.93 (8.009), psychiatric diagnosis 16.63 (8.865), mental retardation 17.15 (9.317). The receiver operating characteristics curve showed that the grand score had a sensitivity of 0.742 and a specificity of 0.773, while the overall cutoff point for both sexes was 23.5 (23.5 for males and 22.5 for females) (Figure 1). The Scheffé test results showed that the "inattention-restlessness" mean scores of children in the ADHD diagnosis only and the ADHD plus psychiatric diagnosis groups differed significantly (*P*<.001) from that of the children in either the normal (*P*<.001), the psychiatric diagnosis (*P*<.001), or the mental retardation (*P*<.01) groups (Table 3). The mean score of the 'impulsivity-hyperactivity' subscale differentiated between the children with ADHD and children in other groups of the study (*P*<.001) (Table 4). However, the 'impulsivity-hyperactivity' mean scores of the ADHD diagnosis only and the ADHD plus psychiatric diagnosis groups were significantly larger than that of either the normal (*P*<.001), the psychiatric diagnosis ($P<.01$), or the mental retardation ($P<.05$) groups.

DISCUSSION

A valid and reliable behavioral rating scale for screening of children suspected of having ADHD is an essential step toward accurate diagnosis and optimal management. The need for such a scale in Saudi Arabia can hardly be overemphasized. Our results show that the grand total scores obtained by the children on the ADHD Rating Scale (Arabic version) differentiated between the children with ADHD, whether as a pure clinical condition or as a comorbidity, and the children who were either normal or had a psychiatric diagnosis other than ADHD, including the mental retardation diagnosis.

Two prevalence studies on ADHD in Saudi Arabia reported rates of 12% and 16.5%.[7] Regardless of the accuracy of such a high rate of prevalence for this disorder, observations and discussions with various mental health workers and school teachers indicate that manifestations of at least ADHD-like symptoms are common and frequent features among a notable proportion of the childhood population in primary school settings. On the other hand, there is as yet no rating scale for screening ADHD symptoms that has clinically proven validity measurement indices that can validly and reliably discriminate children with ADHD symptoms from normal children and children with such conditions as anxiety, depression, mental retardation, or other childhood mental disorders. The few ADHD rating scales existing in Saudi Arabia are merely translations of foreign rating scales. They have not been sufficiently studied in terms of their validity and reliability measures. For example, none of the local rating scales has a proven validity based on a comparison with a gold standard, such as a valid clinical diagnosis or a similar rating scale with empirically proven validity measures.

The original scale was developed and standardized for obtaining a direct rating of the essential symptoms of the disorder from both parents and teachers.[3] However, ratings were obtained from parents only in this study, a situation that was largely due to logistical constraints such that access to school settings at the time of the study was complicated by official and administrative obstacles. A future replication of the study is recommended whereby ratings are to be obtained from both parents and teachers.

The results of this study indicate that ADHD is not restricted to a particular social strata, family type, family size, or to parents with a certain educational level. For example, it was found that parents who rated the symptoms of their children on the ADHD Rating Scale (Arabic version) above the cutoff for ADHD di-

Table 4. Multiple comparisons of diagnostic group mean scores on the "Impulsivity-Hyperactivity" sub-scale of the ADHD Rating Scale (Arabic Version).

	Normal	ADHD diagnosis only	ADHD+other psychiatric diagnosis	Psychiatric diagnosis
ADHD diagnosis only	a			
ADHD+ psychiatric diagnosis	a	1.000		
Psychiatric diagnosis	b	b	b	
Mental retardation	c	c	c	0.999

ᵃ$P<.001$; ᵇ$P<.01$; ᶜ$P<.05$ (Scheffé Test).

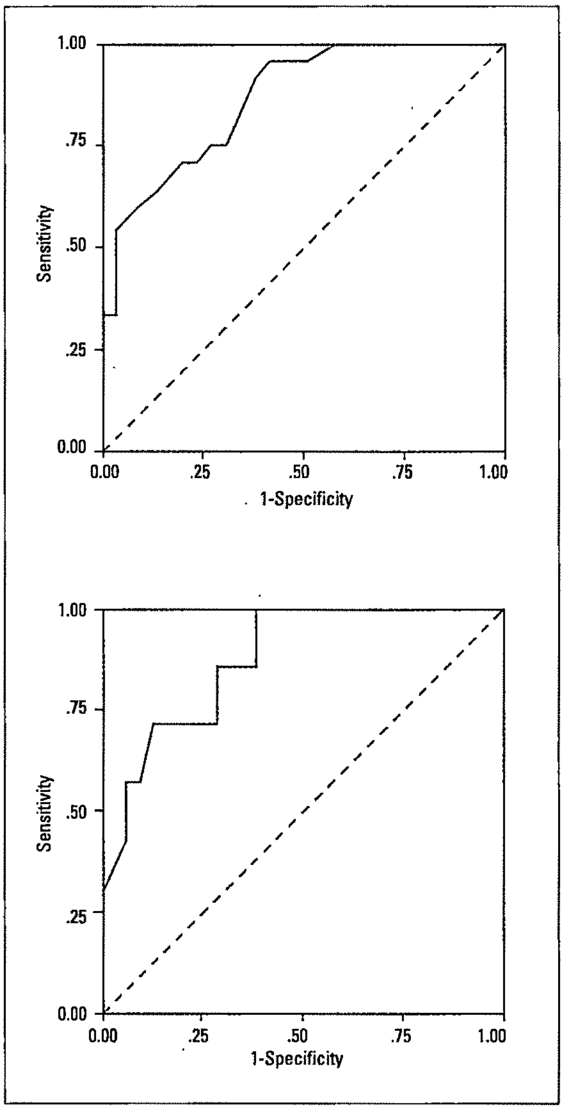


Figure 1. Receiver operating characteristics curves for males (top) and females (bottom). Values along the 45-degree diagonal indicate results no better than chance for detecting disease.

agnosis were of various educational levels, ranging from illiteracy to post-graduate education. This finding also indicates that parents' recognition of the behavioral manifestations of the disorder is irrelevant to their educational level.

Not surprisingly, the study groups differed significantly in terms of the school grade that a child had achieved (i.e., years of schooling). Children who were mentally retarded and children with ADHD combined with another Axis I psychiatric diagnosis (i.e., co-morbidity) had a significantly lower grade level. An examination of the data has shown that the mentally retarded children either did not attend any school, or they attended what is locally termed "special schools" where the mentally retarded children attend 'school time' during daytime with very little to do except playing games, and they usually do not progress from one grade to a higher one.

Although the parents' educational level did not show a significant group difference in this study, a trend was observed for some parents with high educational level to rate their children relatively higher on ADHD symptoms, compared to those with low or no education.[7] This observation is thought relevant to the theoretical assumption that highly educated parents are more likely to belong to middle or high socioeconomic strata and are likely to be more observant and probably more critical of their children's behavioral disturbances, with a lower tolerance for such behaviors, compared to parents in a low socioeconomic stratum and with low or no education. For example, Weckerly, et al[2] found that caregiver years of education was significantly positively associated with the "inattention" but not with the "hyperactivity-compulsivity" symptoms of ADHD in a sample of high-risk youths in public service sectors. However, the sample size of this study is deemed relatively small, such that a larger sample size is recommended in future studies, which may allow for more adequate exploration of the effect of parents' educational level on the way children were rated on the scale.

In this study, the psychiatrist who reached the diagnosis for a child is different from the one who supervised the completion of the data collection form by the parent of the same child. Some of the guardians who rated their children on the ADHD Rating Scale (Arabic version) preferred to complete the scale at home due to time constraints. This arrangement did not seem to have influenced the quality of their rating in any inappropriate way. However, a future similar study would be expected to apply additional controls on the study, specifically by blinding the process of diagnosing children from the process of rating the same children, preferably with inter-rater protocols.

The sample of this study is largely a clinical sample. Future studies on the prevalence of ADHD in the Saudi community, involving children recruited from their community settings, are highly recommended. However, unless a solid screening tool with strong validity indices is established, community screening for prevalence of ADHD may be misleading. Therefore, it is recommended that a future similar study administer the validated ADHD rating scale to a larger number of participants. Such an exercise may re-confirm or modify the cutoff points established in this study.

In summary, the ADHD Rating Scale (Arabic version) successfully differentiated children with a clinically proven ADHD diagnosis from both normal children and children with non-ADHD psychiatric diagnoses that include mental retardation. The "inattention" and "impulsivity-hyperactivity" subscales were equally successful in such a differentiation. The study re-emphasized the importance of developing and validating ADHD rating scales against some solid gold standards before administering them for obtaining prevalence rates of the disorder in communal settings. The acknowledged limitations, such as small sample size and utilization of a rating scale that is probably out-dated, may not overshadow the fact that the study probably provided the clinical and investigative grounds for an improved research work on ADHD in Saudi Arabia in the recent future.

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brief report

Prevalence of exercise-induced bronchoconstriction in teenage football players in Tunisia

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Ann Saudi Med 2009; 29(4): 299-303

BACKGROUND AND OBJECTIVES: Studies on exercise-induced bronchoconstriction (EIB) in team sports are lacking. The aim of this study was to screen for EIB among amateur teenage football players in Tunisia and to compare EIB prevalence between regions.

METHODS: One hundred ninety-six male football players (mean age [SD], 13.5 [0.5] yrs), practicing in three different cities of Tunisia (Tunis, Sousse and Sfax), underwent an outdoor free run of 7 minutes. Forced expiratory volume in one second (FEV_1) was recorded prior to and at 0, 3, 5, 10, 15, 20 and 30 minutes after the run. Players were screened for EIB positivity defined as a greater than 10% decline in FEV_1 from the resting value at any timepoint.

RESULTS: FEV_1 decreased more than 10% in 30% of the players. EIB positivity was more common in Sfax (15.8%) than in Tunis (7.7%) (*P*=.03). Air humidity during the study was higher in Tunis.

CONCLUSION: EIB is prevalent among amateur teenage football players in Tunisia. The prevalence differs between regions and seems to be dependent on air humidity levels.

Exercise-induced bronchoconstriction (EIB) also referred to as exercise-induced airway hyperresponsiveness in athletes, is a common, but often unrecognized condition because it is underdiagnosed, occurring in both known asthmatic and healthy athletes.[1] Sparsely studied, the EIB is defined as the occurrence of a transient airway obstruction, immediately to 30 minutes after vigorous exercise, while exercise-induced asthma is used to describe this condition in subjects who have previously diagnosed respiratory symptoms.[1,2] EIB affects 4% to 20% of the general population and 40% to 90% of asthmatic patients.[1,3] The prevalence of EIB among athletes trained for high level endurance competitions (cross-country skiers, ice skaters, cyclists, swimmers or long distance runners) ranges from 10% to 55%.[1-4] EIB in amateur athletes has not been well documented, but was reported at a lower prevalence of 5.3% in amateur endurance-trained athletes.[5]

The pathogenesis of EIB is not clearly defined, but there is general agreement that inhalation of large volumes of cold, dry air during exercise leads to a loss of heat and water from the bronchial mucosa leading to airway cooling and drying.

The variability in prevalence of EIB depends on the type of exercise, environmental conditions, diagnosis criteria and a previous history of asthma.[8] In Tunisia, asthma prevalence in the teenage non-athlete population has been estimated at 13.2% in Tunis city,[9] but EIB prevalence in teenage athletes has not been evaluated.

The aim of the present study was to estimate the prevalence of EIB and assess the effect of climate on prevalence in teenage high level amateur football players in different regions of Tunisia using a submaximal free running test.

PATIENTS AND METHODS

Paticipants included 196 young male amateur football players in three different regions of Tunisia: 99 in Tunis in the north, 59 in Sousse in the center part of the country and 38 in Sfax in the south. Their mean (SD) age was 13.45 (0.51) years, ranging from 13 to 14 years old. The median range was 13.45. All had 3 to 4 years of training experience. The subjects and their coaches gave verbal consent to study participation. The study was carried out in the afternoon (3 to 6 PM), the coldest part of the day, from December 2002 to March 2003. Age, height and weight were recorded for each footballer.

Pulmonary function testing and measurements were carried out at the training and competition sites of the different teams and under usual environmental conditions. Prior to a test session, all players completed a 10-item medical history questionnaire that focused on asthma symptoms or medication taken, atopy, and EIB symptoms (Appendix 1). Then, each footballer had to perform a submaximal free outdoor running test of 7 minutes. Continuous monitoring of heart rates was obtained with a handheld pulse-meter. Pulmonary function tests were assessed according to the American Thoracic Society (ATS) guidelines10 with a flow-volume spirometer (heated pneumotachograph, Medikro 909, Medikro Oy, Finland) and FEV_1 was determined at each tested time point. Baseline spirometry was followed by an exercise challenge performed in groups of five. Each subject was asked to perform a 2 minute run by increasing the running speed until the heart rate reached 80% to 90% of the predicted maximum heart rate, calculated as 200 minus the age in years, and then asked to maintain this speed over 5 minutes. FEV_1 was recorded at rest and at 0, 3, 5, 10, 15, 20 and 30 minutes after the exercise, and the lowest value from three trials was chosen to represent the FEV_1 in the participant. Predicted values were assessed from spirometric reference values in Tunisian children.[9] EIB was defined as a fall in FEV_1 of at least 10% from the resting value at any time point after exercise, based on ATS guidelines.[10] The percent variability of FEV_1 at each time point was computed as follows:

$[(\text{rest } FEV_1 - \text{lowest post-exercise } FEV_1)/\text{rest } FEV_1] \times 100.$[10]

Table 1. Weather conditions during the study.

	Mean temperature (°C)		Mean humidity (%) Mean temperature (°C)	
	December	January	December	January
Tunis	14.2	12.6	83	81
Sousse	15	13.4	68	68
Sfax	14.2	12.6	65	65

Table 2. Anthropometric and baseline lung function data of subjects with exercise-induced bronchoconstriction (EIB) and controls.

	EIB	No EIB	*P* value
Patients n (%)	20 (10.2)	176 (89.8)	
Age (yr)	13.45 (0.51)	13.43 (0.49)	.86
Weight (kg)	50.65 (9.1)	54.00 (8.9)	.68
Height (cm)	161 (0.07)	165 (0.07)	.016
Baseline mean FEV_1 (%)	91.6 (5.34)	95 (4.4)	.2

Data are presented as mean (SD) unless otherwise indicated. FEV_1: forced expiratory volume in one second.

Measurements of temperature and air humidity were obtained from the national weather center, in the three different cities.

Descriptive statistics are presented as mean and standard deviation. The chi-squared test with Yates correction and non-parametric test of Wilcoxon was used for percentage comparisons, and the *t* test for means comparisons. The level of significance was selected as $P \leq .05$.

RESULTS

All subjects completed the study protocol. Relative humidity was higher in Tunis comparing with Sfax and Sousse (83% vs 65% and 68%) (Table 1). There were no reported signs or symptoms of underlying chronic asthma or EIB. No medication use was reported by the participants. The prevalence of EIB was 30% (59/196) based on a 10% fall in FEV_1. There was no significant difference between football players with and without EIB with regard to age and weight, but subjects with EIB were significantly shorter than negative EIB counterparts (Table 2). Resting FEV_1 expressed in liters per minute was compared to reference values in both groups according to the subject's height established by the following equation: $\ln(FEV_1) = \text{constant} + \text{height coefficient} \times (\text{height})$[10] The frequency of mean FEV_1 at baseline was not different between subjects with and without EIB ($P=.2$) (Table 2).

A fall in FEV_1 was observed in all subjects; 49% had a fall in FEV_1 between 5% and 10% of the rest FEV_1 value. Intergroup comparisons of FEV_1 values showed that subjects with EIB had lower FEV_1 values at rest and at all time points following exercise when compared to EIB negative subjects (Figure 1). EIB-positive subjects experienced significant declines in FEV_1 after exercise. The fall was maximal between the third and fifteenth minute but remained significantly lower than EIB-negative subjects at 30 minutes post exercise.

The prevalence of EIB differed in the three regions, with the lowest rate in the Tunisian team (n=14, 23%)

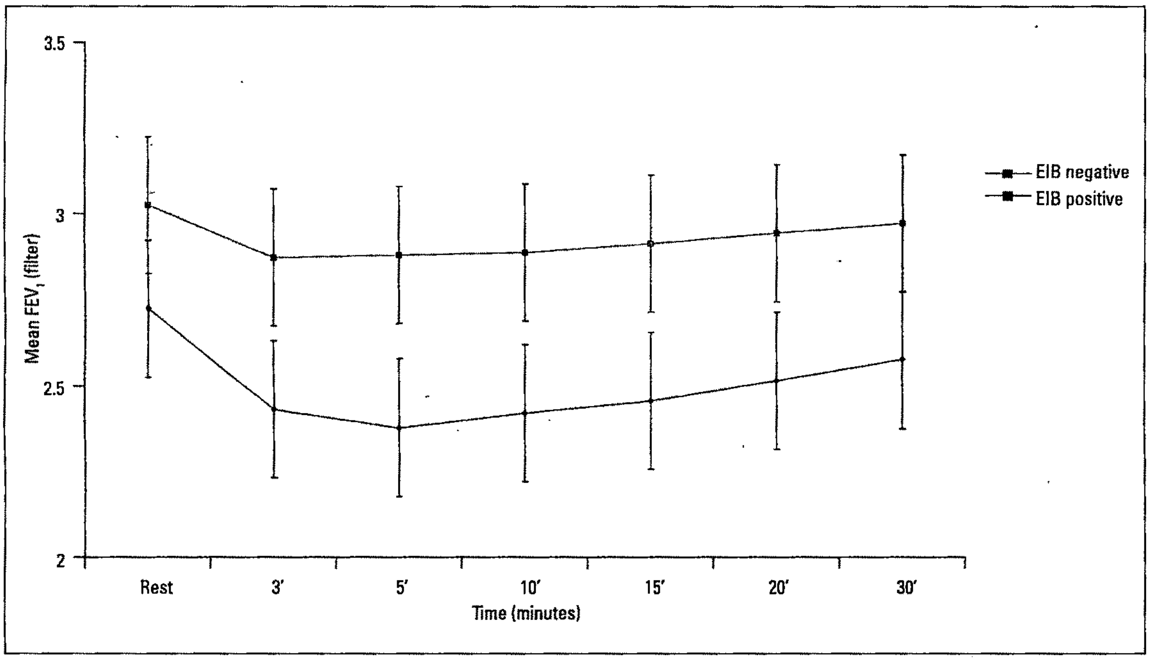

Figure 1. Distribution of FEV$_1$ before and at different times after exercise (0, 3, 5, 10, 15, 20 and 30 min) for football players with or without exercise-induced bronchoconstriction (EIB).

and the highest in the Sfaxian team (n=25, 42%) (P=.03) (Figure 2).

The time points at which the greatest decline of FEV$_1$ occurred in patients with EIB ranged from 3 to 15 minutes, and the distribution was as follows: 20% experienced the greatest decline at 3 minutes postexercise; 40% at 5 minutes; 25% at 10 minutes; and 15% at 15 minutes postexercise.

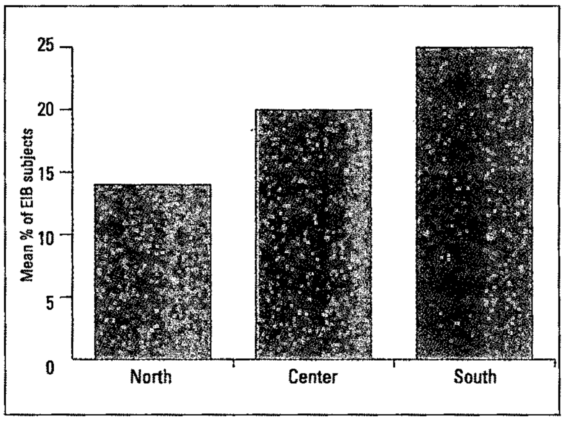

Figure. 2. EIB prevalence in different regions of Tunisia.

DISCUSSION

The current study found a high prevalence (30%) of EIB in apparent healthy football players in Tunisia. The prevalence varied between regions in Tunisia depending on the climate. The high prevalence of EIB is not surprising since numerous studies on highly trained athletes have reported a relatively high prevalence of EIB (Table 3). Initial reports on EIB among athletes included the surprising finding of an 11% prevalence among the US 1984 summer Olympic team athletes.[11] In football players, the prevalence of EIB ranged from 9% to 50%.[12-17] Kukafka et al[14] found a 9% prevalence of EIB among non-asthmatic young football players. A prevalence of up to 50% was reported in subjects who frequently complain of exercise-induced respiratory symptoms.[15]

The prevalence of EIB may be influenced by the value of the decline in FEV$_1$ used to define EIB.[18] Authors agree that to diagnose EIB, a decrease in respiratory flow of at least 10% from baseline is recommended.[12,17-20] To increase specificity, others have employed a more stringent criterion of at least a 15% fall.[14,21,22] In 1999, the ATS put guidelines for methacholine- and exercise-challenge testing criteria[10] recommending a fall in FEV$_1$ of more than 10%. Bronchodilator reversibility to an inhaled β_2-agonist should be documented after a lung function measurement.[2,23] This test was not used in this study, since no player had clinical symptoms and the purpose of this study was not to diagnose exercise-induced asthma, but to assess the prevalence of EIB .

In this study, the comparisons of baseline FEV$_1$ were made according to spirometric reference values

Table 3. Prevalence of EIB/EIA among athletes from published studies.

Authors (Ref)	Method	Condition	Population: Prevalence
Voy[12]	Questionnaire	EIA, asthma	American Olympic summer athletes: 11%
Mannix[18]	Exercise test	EIB	Competitive figure skaters: 35%
Feinstein[16]	Exercise test	EIB	Male football players: 19%
Sodal[17]	Methacholine BHR	BHR	Female soccer players: 35.5%
Ross[23]	Reversibility test	Reversibility	Canadian football players: 56%
Schoene [13]	Exercise test	EIB	Male athletes: 10% Female athletes: 26%
Kukafka[14]	Exercise test	EIB	Young football players: 9%
Brudno[22]	Exercise test	EIB	Scholars: 47%

EIA: exercise-induced asthma, EIB: exercise-induced bronchoconstriction, BHR: bronchial hyperresponsiveness.

established for healthy Tunisian children.[24] Subjects in the present study with EIB were significantly shorter than EIB negative counterparts; in fact, height as a surrogate for smaller lungs and therefore smaller airways may be an important correlative factor to explain EIB prevalence in shorter subjects, in the opinion of the present authors. Concerning the lack of asthma signs reported in this study, we propose the hypothesis that young footballers selected to compete in national teams might not report symptoms of asthma or EIB since asthma suspicion often leads to exclusion by the coach.

Different challenge tests can be used to assess EIB. Pharmacological challenge tests, such as methacholine challenge, have low sensitivity for EIB diagnosis.[25-27] Sport-specific exercise in the field with respect to the standardization of both the workload and the environmental conditions of temperature and humidity is recommended in athletes.[27] Nevertheless, the gold standard to assess EIB in elite athletes is the eucapnic voluntary hyperpnea (EVH) with dry air.[26] An alternative to the EVH challenge is the hyperosmotic challenge test, either with hypertonic saline or inhaled mannitol dry powder, which have both a high sensitivity (96%) and specificity (92%) for EIB.[25,26]

EIB prevalence may vary with seasons.[1] It is well documented that EIB is more prevalent when using an exercise challenge with cold dry air and during pollen season.[3,15,28-30] For this reason, we conducted this study during winter and part of spring.

Relative humidity is an important factor contributing to EIB occurrence.[31] The difference in the EIB among subjects in different cities in different parts of the country can probably be explained by humidity being consistently lowest in the southern region (by nearly 20%) vs the northern region. Tunisia is located on the Mediterranean Sea, and has high rates of humidity throughout the year, so humidity levels recorded were higher than those recommended by the American Thoracic Society (50%), which in itself may protect against EIB, so the reported 30% rate of EIB may be an underestimation.

In conclusion, our findings suggest that EIB may be common in athletes. The prevalence difference observed between regions may be explained by different levels of humidity. Screening for EIB and therapeutic follow-up are reasonable considerations for athletes to train at the necessary intensity and to be able to achieve peak performance.

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1. Do you smoke cigarettes, cigar, or pipe?
2. Does anyone in your family have asthma?
3. Does anyone living in your household smoke at home?
4. Are you allergic to inhalants allergens, such as dust, pollen, or animal hair?
5. Do you take any medications on a regular basis (steroids, birth control pills, etc)?
6. Have you ever been told that you have asthma or exercise-induced asthma, even as a child?
7. Have you ever had wheezing, chest tightness, itchy eyes or nose?
8. Do you have trouble with breathing or would you experience coughing after running 1 mile and resting for 10 or 15 min?
9. Have you ever missed school, work, or practice because of chest tightness or cough or wheezing or prolonged shortness of breath?
10. Do you have trouble breathing or do you cough during or after activity?

Appendix 1. Medical history questionnaire.

brief report

The validity and reliability of the Arabic version of the EQ-5D: a study from Jordan

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Ann Saudi Med 2009; 29(4): 304-308

BACKGROUND AND OBJECTIVES: EQ-5D is a generic measure that permits comparisons in quality of life across disease states, and which may provide useful data for health policy and resource allocation decision-making. There are no published reports on the acceptability and psychometric properties of the EQ-5D in the Arabic language. We therefore investigated the validity and reliability of the Arabic translation of the EQ-5D in Jordan.

METHODS: The study was conducted on a convenience sample consisting of consecutive adult Arabic-speaking outpatients or visitors attending a university teaching hospital. Subjects were interviewed twice using a standardized questionnaire containing the EQ-5D, Short Form 36 Health Survey (SF-36). To assess the validity of the Arabic version of the EQ-5D, ten hypotheses relating responses to EQ-5D dimensions or the visual analogue scale (EQ-VAS) to SF-36 scores or other variables were examined and test-retest reliability was assessed.

RESULTS: The study included 186 subjects who had a mean age of 45.3 years and included 87 (47%) females. The major problem reported in more than 102 (55%) of the subjects was anxiety/depression. All of the ten a-priori hypothesis relating EQ-5D responses to external variables were fulfilled. Cohen's κ for test-retest reliability (n=52) ranged from 0.48 to 1.0.

CONCLUSION: The Arabic translation of EQ-5D appears to be valid and reliable in measuring quality of life in Jordanian people.

Measurement of health-related quality of life (HRQL) has become an imperative in clinical trials and disease management programs for a variety of diseases. HRQL can be considered a major outcome in clinical trials in the absence of objective measures. In Jordan, where Arabic is the first language, conducting clinical trials is difficult due to the lack of validated Arabic translations or versions of quality of life instruments. The EQ-5D is a standardised generic instrument for use as a measure of health and quality of life outcomes. Applicable to a wide range of health conditions and treatments, it provides a simple descriptive profile and a single index value for health status. The EQ-5D is now available in most major languages with cultural adaptations.[1-3] There are no published reports on the acceptability and psychometric properties of the EQ-5D iin the Arabic language, which is the first language for more than 300 million people. Using a convenience sample of lay people we therefore investigated the validity and reliability of the Arabic version of the EQ-5D in Jordan as a prelude to a future population-based valuation of health states. Jordan is a small country in the Middle East with a population of over 5 million people. This study is part of a larger project aiming at developing, translating and adapting important instruments and questionnaires into Arabic.

METHODS

The study group was a convenience sample that consisted of consecutive adult Arabic-speaking outpatients or visitors attending the University of Jordan hospital in the period between June to August 2007. The inclusion criteria were that the subject should be an adult Jordanian and should have no obvious cognitive deficit. The hospital is located at the center of Amman, the capital of Jordan, and is considered one of the oldest and largest hospitals in Jordan serving more than 0.5 million people every year. The study site was ideal for testing the instrument as it serves a diverse group of patients from all over the country.

Translation and cross-cultural adaptation was done according to the EuroQol group's guidelines.[4] Two in-

Table 1. General characteristics of the study subjects.

	n (%)
Mean age (SD, range)	45.3 (15.9, 19-77)
Age ≥60 years	45 (24.2)
Female	87 (46.8)
Participants with a chronic disease	95 (51.1)
Education level	
Not educated	7 (3.8)
Primary	39 (21.0)
Secondary	23 (12.4)
University/college*	113 (60.8)
Missing data	4 (2.2)
Marital status	
Single	49 (26.3)
Married	129 (69.4)
Widowed	5 (2.7)
Missing data	3 (1.6)
Profession	
Employed	62 (33.3)
Unemployed	3 (1.6)
University student	49 (26.3)
Housewife	53 (28.5)
Retired	16 (8.6)
Missing data	3 (1.6)

* Includes those who are still university students, see under profession.

dependent translators performed forward translation, followed by backward translation by another two translators. When the consensus version was determined, cognitive debriefing was done by ten laypersons. They underwent a structured interview to assess understandability and ease of completion of the Arabic EQ-5D.

The translation process was smooth and straightforward. The translators only disagreed on the translation of "discomfort" during the forward translation process as it can be translated into several closely related words. A discussion session was conducted until the translators agreed on the most appropriate translation. During the interview with the ten laypersons, they reported no concerns with the phrasing of the Arabic EQ-5D. In general, the instrument was very easy to complete and clear to all readers.

The study was approved by the University of Jordan Academic and Research Committee. All participants were interviewed by trained research assistants using a questionnaire containing the Arabic version of the EQ-5D and the short form health survey (RAND SF-36-Arabic version).[5] Demographic data were also collected using a standard questionnaire. A random sample was then chosen, given a copy of the EQ-5D and re-interviewed over the phone using the EQ-5D after 2 to 4 weeks to assess test-retest reliability.

The EQ-5D6 consists of a self classifier with five single item health dimensions, each with three response levels, and a visual analogue scale (EQ-VAS). Both the health state descriptors and the visual analogue scale of the perceived health state of the Arabic version of the EQ-5D were used in the current study. The SF-36 is a validated,[5,7,8] 36-item instrument measuring perceived health in eight dimensions with higher scores (range 0 to 100) reflecting better perceived health.

Known-groups construct validity[9] of the EQ- 5D self-classifier and EQ-VAS was examined by testing ten priori hypotheses based on the literature or clinical experience. Hypotheses relating EQ-5D dimensions to other variables were:

1. Subjects reporting problems for any EQ-5D dimension would have lower scores for all SF-36 scales;[10]
2. Subjects reporting problems for EQ-5D mobility, self-care, usual activities or pain/discomfort dimensions would have larger score reductions for SF-36 physical functioning (PF), role limitation due to physical problem (RP) and bodily pain (BP) scales than for role limitation due to emotional problem (RE) and mental health (MH) scales;
3. Similarly, subjects reporting problems for the EQ-5D anxiety/depression dimension would have larger score reductions for SF-36 RE and MH scales;
4. Subjects with mobility, self care, or usual activities problems should have their lowest score in role limitation due to a physical problem;
5. Elderly (age ≥60 years) or
6. Subjects with chronic diseases should report more problems than other subjects.

Hypotheses for the EQ-VAS were:

7. EQ-VAS scores would be higher in subjects reporting better global health measured using a 5-point scale (i.e lower score on the first question of

Table 2. Distribution of responses to EQ-5D dimensions.

EQ.5D dimension	Response (%)		
	No problem	Moderate problem	Extreme problem
Mobility	127 (68.3)	58 (31.2)	1 (0.5)
Self care	172 (92.5)	12 (6.3)	1 (0.5)
Usual activities	125 (67.2)	53 (28.5)	8 (4.3)
Pain/ discomfort	87 (46.8)	90 (48.4)	9 (4.8)
Anxiety/ depression	84 (45.2)	93 (50)	9 (4.8)

the SF-36);[11,12]

8. EQ-VAS scores would correlate negatively with increasing age;[12-13]
9. Females will report lower (worse) EQ-VAS scores;
10. Subjects with chronic disease will report lower (worse) EQ-VAS scores than those without.

Hypothesized trends were tested as appropriate depending on the type of data and distribution using the chi-square, the Fisher exact test, *t* test, the Mann-Whitney test, and Pearson or Spearman correlation coefficients. To minimize false-positive tests of significance, a significance level of $P<.01$[14] should be used as a criterion for hypothesis fulfillment. Test-retest reliability of EQ-5D dimensions was investigated using the Cohen κ. According to Landis and Koch,[15] κ coefficients of less than 0.0 are poor, 0.0 to 0.20 are slightly poor, 0.21 to 0.40 are fair, 0.41 to 0.60 are moderate, 0.61 to 0.80 are substantial, and 0.81 to 1.00 are almost perfect. Data were analyzed with SPSS for Windows (version 9, SPSS Inc, USA).

RESULTS

During the study period, 200 subjects were asked to participate and only 14 refused. The main reason behind refusal was lack of time. The demographic and clinical characteristics of those who refused to participate were similar to the study subjects. One hundred eighty-six subjects completed the baseline questionnaires. Table 1 shows the general characteristics of the subjects. Table 2 shows distribution of responses to EQ-5D dimensions. There was only one missing item from the self care and the usual activities dimensions indicating the practicality and simplicity of the translated version. Among five dimensions of the EQ-5D, the proportion of having any problem was highest for anxiety/depression with 102 (55%) subjects reporting having moderate or extreme problems. The mean EQ-VAS score was 72.2 (SD 15.5).

Cronbach's α was 0.75 indicating that the EQ-5D has an acceptable internal consistency.

Fifty-two subjects (28.0%) participated in the follow-up telephone interview, with a 3-week median interval (interquartile range: 2 to 4 weeks). Cohen's κ values for EQ-5D mobility, self care, usual activities, pain/discomfort and anxiety/depression items were 0.66, 1.0, 0.48, 0.66, and 0.48 respectively ($P\leq.001$ for all dimensions). Intraclass correlation coefficient for the EQ-VAS between the two periods was 0.78.

All of the four hypotheses relating EQ-5D dimensions to SF-36 scales were fulfilled (Tables 3 and 4). Subjects reporting moderate or extreme problems for EQ-5D dimensions had lower SF-36 scores than those without such problems. Similarly subjects reporting problems for EQ-5D mobility, self-care, usual activities or pain/discomfort dimensions had larger score reductions for SF-36 PF, RP and BP scales than for RE and MH scales. When subjects were grouped by their responses to the EQ-5D anxiety/depression dimension, the difference in scores for the SF-36 MH and RE scales was larger than that for all other scales. In addition, subjects with mobility, self care, or usual activities problems had their lowest score in role limitation due to physical problem. Elderly participants (n=45) and those with at least one chronic medical problem (n=95) had significantly reported more problems in all of the EQ-5D dimensions apart from anxiety/depression (Table 4).

On the other hand, all four hypotheses for the EQ-VAS were fulfilled (Table 5). The EQ-VAS was positively correlated with global health (lower score on SF-1 indicates better health) and negatively correlated with increasing age. Participants with at least one chronic problem had significantly lower results than those without. Females scored lower on the EQ-VAS, but this was significant only at the 0.05 level.

DISCUSSION

This is the first report on the reliability and validity of the EQ-5D in Arabic. All of the ten priori hypotheses were fulfilled, suggesting that the translation has properties similar to those of other validated EQ-5D versions. Internal consistency of the instrument was also found to be acceptable. We also found evidence to support test-retest reliability of the EQ-5D self-classifier, with Cohen's κ being moderate to perfect (0.48-1.0). The κ values in our study were in general better than those reported in previous studies of subjects after stroke using EQ-5D (Cohen's κ: 0.63-0.80, 3-week, n=234)16

Table 3. Mean SF-36 scores for subjects in different EQ-5D dimensions (hypothesis 1 to 4).

EQ-5D dimension	N	PF mean (SD)	RP mean (SD)	BP mean (SD)	GH mean (SD)	VI mean (SD)	SF mean (SD)	RE mean (SD)	MH mean (SD)
Mobility									
No problem	127	89.1 (11.8)[a]	79.7 (33.6)[a]	80.4 (19.9)[a]	66.8 (14.9)[a]	59.4 (19.6)[a]	79.7 (20.5)[a]	68.7 (41.1)[b]	67.4 (19.6)
With problem	59	50.2 (24.5)	26.7 (35.6)	49.6 (20.8)	46.2 (15.2)	44.1 (19.6)	56.4 (24.0)	53.1 (44.7)	63.2 (18.6)
Self care									
No problem	172	80.5 (20.7)[a]	67.0 (40.8)[a]	73.2 (23.4)[a]	61.9 (16.6)[a]	56.1 (20.4)[a]	74.5 (22.3)[a]	65.3 (42.6)	66.4 (19.5)
With problem	13	26.9 (21.6)	11.5 (21.9)	37.8 (19.7)	36.9 (18.3)	33.8 (14.3)	41.8 (29.9)	64.2 (44.2)	62.5 (17.4)
Usual activity									
No problem	125	88.4 (13.3)[a]	82.0 (31.2)[a]	81.3 (19.0)[a]	67.2 (14.6)[a]	60.0 (19.7)[a]	80.6 (19.8)[a]	69.6 (40.6)[c]	67.2 (19.7)
With problem	60	53.9 (25.4)	23.3 (34.1)	49.0 (21.0)	46.7 (15.5)	43.8 (18.5)	56.2 (23.6)	52.3 (45.3)	63.5 (18.3)
Pain/ discomfort									
No problem	87	90.5 (12.1)[a]	84.8 (28.6)[a]	86.7 (16.4)[a]	69.2 (13.6)[a]	63.2 (19.2)[a]	82.3 (18.1)[a]	68.2 (42.2)	68.1 (19.5)
With problem	99	64.8 (26.8)	43.7 (42.9)	45.6 (22.2)	52.4 (17.3)	47.0 (19.2)	63.6 (25.5)	60.0 (43.1)	64.4 (19.1)
Anxiety/ depression									
No problem	84	81.1 (19.5)[b]	73.2 (39.9)[c]	78.0 (21.8)[a]	65.4 (14.8)[a]	63.2 (17.3)[a]	80.3 (21.7)[a]	81.8 (32.9)[a]	76.0 (14.2)[a]
With problem	102	73.3 (28.0)	56.4 (42.3)	64.6 (25.5)	56.1 (18.9)	47.5 (20.8)	60.9 (24.2)	47.0 (44.5)	52.0 (19.2)

PF: physical functioning, RP: role limitation due to physical problem, BP: bodily pain, GH: general health, VI: vitality, SF: social functioning, RE; role limitation due to emotional problem, MH: mental health; [a]$P<.001$; [b]$P<.05$; [c]$P<.01$.

Table 4. Relationships between responses to EQ-5D dimension and other variables (hypothesis 5 and 6).

EQ-5D dimension vs other variables	N (%) with mobility problems	N (%) with self care problems	N (%) with usual activities problems	N (%) with pain/discomfort problems	N (%) with anxiety/ depression problems
Age ≥60	26 (57.8)[a]	9 (20)[a]	24 (54.5)[a]	36 (80)[a]	22 (48.9)
Age <60	32 (22.9)	4 (2.9)	35 (25)	62 (44.3)	79 (56.4)
Participants with chronic problems	51 (53.7)[a]	12 (12.6)[b]	44 (46.8)[a]	71 (74.7)[a]	56 (58.9)
Participants without chronic problems	8 (8.8)	1 (1.1)	16 (17.6)	28 (30.8)	46 (50.5)

[a]$P<.001$; [b]$P<.01$

and in those with rheumatic diseases (Cohen's κ: 0.29-0.61, 1-week, n=52).[3] The significant and reasonably high intraclass correlation coefficient obtained in the EQ-VAS reliability study (0.78) demonstrates that the EQ-VAS is a feasible measure of self-reported health.

The results have demonstrated that the major problem reported by 55% of participants was anxiety/depression. Anxiety and depression are commonly associated with the etiology of many diseases including asthma, diabetes and hypertension. This reuslt is very important in the view of the large prevalence of diabetes and hypertension in Jordan, which exceeds 25%.[17]

We have utilized the Arabic version of the EQ-5D in several clinical settings including diabetes, rheumatoid arthritis and allergic rhinitis; the instrument was found to be of high clinical value and was strongly correlated with the clinical indicators. This indicates that the Arabic version of the EQ-5D is externally valid. It should be noted that the participants have completed the EQ-5D with the help of a research assistant. EQ-5D is a very simple instrument; therefore we think there will not be any major difference in the results if the EQ-5D was self administered.

One study limitation was that we used a convenience sample, which may limit the generalizability of the results. This limitation was obvious as the sample was characterized by a high level of education. However; this study is a pilot investigation and we hope in the near future to conduct a population-based investigation. It would have been more appropriate to validate the EQ-5D using a similar utility measure rather then using the SF-36. However, in our case this was not possible as currently the SF-36 is the only available well validated and well translated generic QOL instrument in the Arabic language.

Table 5. Correlation between EQ-VAS score and other variables (hypothesis 6-10).

EQ-VAS dimension vs other variables	Correlation	Mean (SD)
EQ-VAS score vs SF-1	-0.83[a]	NA
EQ-VAS score vs age	-0.54[a]	NA
EQ-VAS score vs gender		
Female	NA	76.7 (16.3)[b]
Male	NA	81.4 (14.4)
EQ-VAS score vs presence of chronic problems		
Participants with chronic problems	NA	71.5 (15.8)[a]
Participants without chronic problems	NA	87.2 (10.1)

[a]$P<.001$; [b]$P<.05$

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case report

Purine nucleoside phosphorylase deficiency in two unrelated Saudi patients

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Ann Saudi Med 2009; 29(4): 309-312

Purine nucleoside phosphorylase (PNP) deficiency is a rare autosomal recessive metabolic disorder that results in combined immunodeficiency, neurologic dysfunction and autoimmunity. PNP deficiency has never been reported from Saudi Arabia or in patients with an Arabic ethnic background. We report on two Saudi girls with PNP deficiency. Both showed severe lymphopenia and neurological involvement. Sequencing of the PNP gene of one girl revealed a novel missense mutation Pro146>Leu in exon 4 due to a change in the codon from CCT>CTT. Expression of PNP (146L) cDNA in *E coli* indicated that the mutation greatly reduced, but did not completely eliminate PNP activity.

Purine nucleoside phosphorylase (PNP) deficiency (OMIM 164050) is a rare autosomal recessive disorder of the purine metabolic pathway that results in combined immunodeficiency with a profound T-cell defect and variable B-cell dysfunction. It is also associated with neurologic dysfunction in about two thirds of patients and autoimmunity in about one third.[1-3] PNP deficiency was first described by Giblett et al in 1975 shortly after their discovery of a deficiency of another enzyme of the purine metabolic pathway, adenosine deaminase (ADA).[4] PNP catalyzes the reversible degradation of inosine and deoxyinosine to hypoxanthine and guanosine, and deoxyguanosine to guanine. When PNP activity is absent or greatly diminished, deoxyguanosine triphosphate is thought to accumulate in the mitochondria, which inhibits ribonucleotide reductase and mitochondrial DNA repair. This leads to increased sensitivity of T lymphocytes to DNA damage and apoptosis during thymus selection. PNP is encoded by six exons spanning 7.5 kb of chromosome 14q13. Approximately 17 disease-causing mutations in the PNP gene have been reported, and the somewhat variable course of the disease associated with PNP deficiency may be related to this genetic heterogeneity.[5]

Less than 50 patients with PNP deficiency have been reported in the literature. To our knowledge, PNP deficiency has never been reported in patients from Saudi Arabia or in patients with an Arabic ethnic background. We report clinical and immunologic findings in two unrelated Saudi girls with PNP deficiency. One of these patients was found to be homozygous for a novel PNP gene mutation.

CASE 1

A 2-year-old Saudi girl was referred to King Khalid University Hospital with history of recurrent chest infections. She had three chest infections. The first at 11 months of age that was treated with oral antibiotics, while the second and third required prolonged courses of intravenous antibiotics. She also had chronic diarrhea, watery, 3 to 4 times per day, and persistent since she was 9 months of age. There was a history of intermittent anemia and leukopenia; she had received a blood transfusion 3 weeks prior to presentation. The patient's parents were first cousins. She has two healthy brothers who are 4 years and 8 months of age. One cousin died at 1 year of age after extensive chicken pox infection.

On examination, the patient appeared poorly nourished and growth parameters were all below the third percentile. A BCG scar was absent (the patient received BCG vaccine on day one of life). She had oral thrush and pus draining from the right ear. Chest examination revealed bilateral coarse crackles. CNS exam revealed a global developmental delay corresponding to about 9 months of age and universally decreased muscle tone.

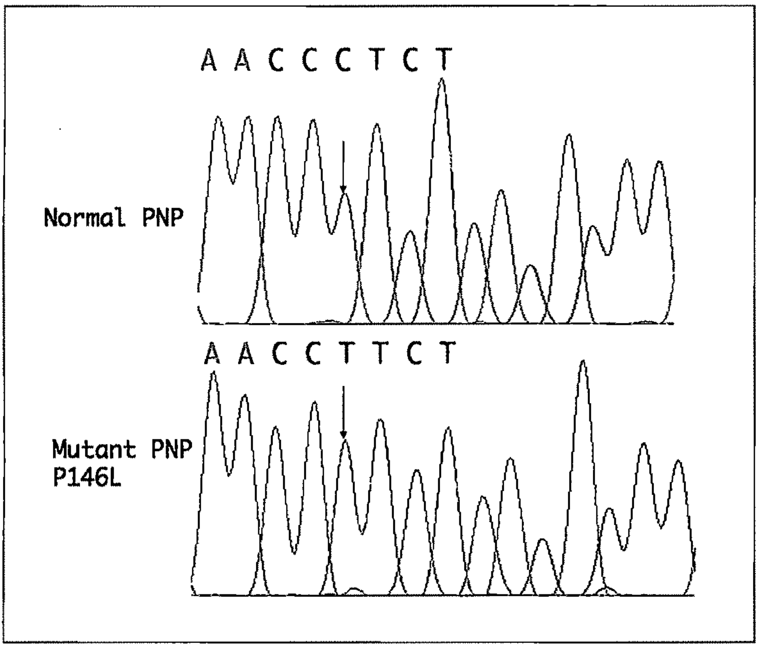

Figure 1. Sequencing of PNP gene from case 1 revealed a novel missense mution Pro146>Leu in exon 4 due to a change in the codon from CCT>CTT.

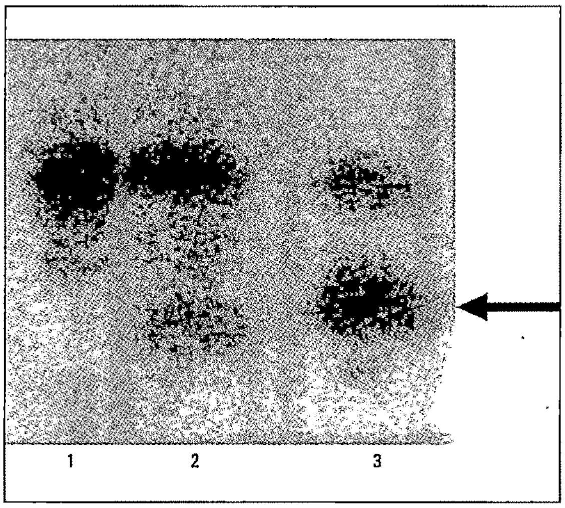

Figure 2. Histochemical in situ assay for PNP activity of recombinant wild type and P146L mutant human PNP, following expression in *E coli*. Lanes contained approximately equal amounts of extract protein. Lane 1, untransformed *E coli* Sϕ3834 (control). Lane 2, *E coli* Sø3834 transformed with 146L (mutant) PNP. Lane 3, *E coli* Sø3834 transformed with 146P (wild type) PNP. The upper staining band is due to *E coli* PNP. The arrow indicates the position of human PNP.

Investigations showed WBCs of 1300/mm^3, an absolute neutrophil count of 510 /mm^3, absolute lymphocyte count 420 /mm^3, hemoglobin of 11.3 g/dL, and platelets of 506x103/mm^3. Bone marrow aspiration revealed a hypercellular active marrow with no dysplasia. Immunoglobulin levels were all elevated: IgG 1877 mg/dL, IgM 366 mg/dL, and IgA 297 mg/dL. Lymphocyte subset enumeration and proliferation responses are shown in Table 1. Uric acid was 62.6 μmol/L (normal range 130-320 μmol/L). PNP enzyme activity was measured by a radiochemical method,[6] as adapted for measuring activity in eluates of dried blood spots on filter paper[7] and it was 324 nmol/L (normal 1336±441). The low level of PNP activity detected, at least partly, reflected the recent blood transfusion that the patient had received because of her anemia.

CASE 2

The second patient was referred to King Faisal Specialist Hospital at 2 years of age because of recurrent chest infections that required multiple hospital admissions for treatment with intravenous antibiotics. Her most recent chest infection was complicated by empyema. There was no history of chronic diarrhea. Her parents were first cousins. She has two brothers and one sister who are alive and well. Another sister died at 3 years of age from extensive chicken pox infection.

On examination, all her growth parameters were below the third percentile. She had delayed motor milestones. Speech was appropriate for age. The tonsils were absent. The remaining systemic examination was normal. Investigations showed WBCs of 4270/mm^3, an absolute neutrophil count of 2540/mm^3, absolute lymphocyte count 618/mm^3, hemoglobin of 9.7 g/dL, and platelets of 643x103/mm^3. Immunoglobulin levels showed IgG 1000 mg/dL (N), IgM 20 mg/dL (low), and IgA 14 mg/dL (normal). Antibody response titer to tetanus was 13.48 IU/mL (protective level>0.17 IU/mL). Lymphocyte subset enumeration and proliferation responses are shown in Table 1. Erythrocyte PNP enzyme activity was undetectable. Unfortunately, material for genotype analysis was not available at the time of diagnosis and the patient was lost to follow-up.

Both patients were vaccinated with BCG, OPV and MMR among other first year killed vaccines (DTP, HIB and Hep B) with no complications.

Mutation analysis

Genomic DNA was prepared from blood samples of patient 1 by standard methods. The exons and intron-exon boundaries of the PNP gene were amplified in 6 separate segments spanning exon 1, exon 2, exons 3-5,

Table 1. Immunological investigation data for the two patients.

		Patient 1	Patient 2	Normal range
Lymphocytes Subsets enumeration /mm^3	-CD 3	385	314	1400-8000
	-CD 4	106	167	900-5500
	-CD 8	263	18	400-2300
	-CD 19	311	58	600-3100
	-CD 16/56	147	231	100-1400
Lymphocyte proliferation responses	-PHA (cpm)	2343	14247	90553-117987
	-Con A (cpm)	1443	10350	78412-105150
	-PWM (cpm)	2934	8705	45008-53536
Enzyme activity	PNP nmol/hr/mg	324	0	1336 (±441)

cpm: counts per minute.

exon 6 and the promoter region. The resulting PCR fragments were sequenced on an ABI 3730 DNA Analyzer (Applied Biosystems, USA).

The primers used for the polymerase chain reactions were:

PNPex1:
5'(+) TCAGTTCAGCATAGCGGAG
5'(-) TCCACTGTCCCTAACACAC
PNPex2:
5'(+) TGCCTCAGTATACCTGCCAG
5'(-) GTCTTCAGTGAAATGCTAGGTC
PNPex3-5:
5'(+) AGCAGAGCGAGTAACTCAC
5'(-) TTCCTACTCCTTCCCCTTCC
PNPex6: 5'(+) TACAGGTGTGAACCACTGC
5'(-) AAGAAAGTGGGAAAGGTGAAG
PNPprom:
5'(+) CGATGAGCCTGCTCCGGTGT
5'(-) TCTAGGACCCCGGAATTCTT

Expression analysis

PNP 146L cDNA was generated using the wild type PNP (146P) cDNA in the pZ vector as template and the Quick Change Mutagenesis kit from Stratagene.

The primers used to introduce the mutation were:

PNP146L:
5'(+) TTCAGTGGTCAGAACCTTCTCAGA GGGCCCAAT
5'(-) ATTGGGCCCTCTGAGAAGGTTCTGA CCACTGAA

The wild type (146P) and mutant (146L) PNP cDNAs were expressed in *E coli* Sϕ3834 essentially as described for human adenosine deaminase.[8] Human PNP activity in extracts of transformants was analyzed histochemically after electrophoresis of bacterial lysates on cellulose acetate strips as described.[6] In situ staining was also performed as described for adenosine deaminase, except that inosine was used as the substrate and exogenous PNP was omitted.

Sequencing of the amplified exons and intron-exon boundaries of the PNP gene from genomic DNA from patient 1 revealed a novel missense mutation Pro146>Leu in exon 4 due to a change in the codon from CCT>CTT (Figure 1). Expression in *E coli* of human PNP cDNA carrying either the wild type PNP sequence or the P146L mutation revealed that the mutant protein had some residual PNP activity (Figure 2). The method used to assess the activity of the mutant enzyme is semiquantitative, but these results suggest that the mutation probably does not completely eliminate PNP activity.

DISCUSSION

PNP deficiency is one of the least common primary immunodeficiency diseases. Seventeen different mutations in 23 unrelated individuals have been described so far.[5] Mutations of C or G nucleotides of Arg at positions 58 or 234 were most common (8/23). The clinical presentation of PNP deficiency is variable, but prognosis is poor, and without restoration of immune function most patients die from complications related to immunodeficiency.[1-3] There have been no systematic studies of the genotype/phenotype correlation in PNP deficiency, but there is evidence of such correlation in its counterpart, ADA deficiency.[8] The novel P146L missense mutation identified in patient 1 has some residual catalytic activity when expressed in *E coli.* By analogy with ADA deficiency, it is possible that this mutant allele might result in a somewhat milder clinical phenotype.

T-cell lymphopenia, recurrent infections, and neurologic findings should raise the suspicion of PNP deficiency, particularly if these are associated with low serum or urinary uric acid level (although the latter is not universally found).[9] The diagnosis is usually established by measurement of PNP enzyme activity in red cells or blood mononuclear cells. Elevated serum or urinary levels of inosine and guanosine are confirmatory.[6] Although B lymphocyte numbers have been normal in most cases, both of our patients had low B-cell numbers. However, patient 1 had high immunoglobulin levels, which may indicate B-cell dysregulation due to T-cell deficiency, rather than adequate B-cell function. Specific antibody titer to tetanus was normal in patient 2, which is not unusual to find in this disorder.[1]

Neurologically, both patients had motor developmental delay, a frequent feature of the disease. Various neurological abnormalities have been described including spastic diplegia or tetraplegia, ataxia, behavioral difficulties and mental retardation.[4] Autoimmune phenomena occur in about one third of patients, mainly hemolytic anemia, thrombocytopenia and neutropenia. Patient 1 presented with relapsing neutropenia that was most probably autoimmune in nature; patient 2 had no evidence of autoimmunity.

In conclusion, this is the first description of Saudi patients with PNP deficiency, including one with a novel disease-causing mutation in the NP gene in one case. T lymphopenia, recurrent infections, and neurologic findings should raise the suspicion of PNP deficiency, especially with a history of parental consanguinity.

Acknowledgment

This work was supported by NIH Grant DK20902 to M. Hershfield. The case report was presented and published as an abstract in the annual meeting of the American Academy of Allergy, Asthma, and Immunology in 2006. Please see Journal of Allergy and Clinical Immunology. 2006;117(2):S173.

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case report

Forced eye closure-induced reflex seizure and non-ketotic hyperglycemia

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Ann Saudi Med 2009; 29(4): 313-315

We report an uncommon case of 53-year-old female patient with partial seizure induced by forced voluntary eye closure due to non-ketotic hyperglycemia. The initial laboratory tests showed an elevated blood glucose level of 550 mg/dL but no evidence of ketosis. Brain magnetic resonance imaging was normal. When the blood glucose levels decreased slowly to about 150 mg/dL in five days, the seizures ended completely. No anticonvulsants were used. Since seizures are generally refractory to antiepileptic medication, control of blood glucose is essential.

Reflex epilepsy is a rare form of epilepsy that develops as a result of certain specific stimulations. The most frequent form of reflex epileptic seizures occur with visual stimuli.[1-3] Reflex seizures induced by non-visual stimuli are rarely reported. Seizures may also be evoked by other activities such as decision making, thinking, calculations, reading and writing, eating, listening to music, proprioception and hot water.[4] We report an uncommon case of a middle-aged diabetic patients presenting with uncontrolled diabetes and partial seizures induced by forced voluntary eye closure.

CASE

A 53-year-old female with poorly controlled diabetes mellitus (DM) was brought to the emergency department with focal motor clonic seizures induced by forced voluntary eye closure due to rubbing her eyes. During hospitalization it was observed that seizures began when she closed her eyes strongly. Every time she repeated the eye closure the seizures recurred. The seizures started two days previously and occurred with each forced voluntary eye closure. She had no seizure with spontaneous eye blinking or sleeping, or with horizontal, vertical or rotatory eye movements. The seizures occured in the left orbicularis oculi, and then spread to the ipsilateral angularis oris and upper extremity, turning to the left side of the head. They lasted 2 to 3 minutes. The patient did not lose consciousness during seizures. She had had type 2 DM for eight years and her past medical history revealed no other significant disease. She had no history of seizures or other neurological disorder. She was using only insulin as her medication. The physical examination, including the neurological examination of the patient, revealed no abnormality. Her visual acuity, pupil reactions to light and eye movements were normal. The laboratory tests showed an elevated blood glucose level of 550 mg/dL but no evidence of ketosis. Serum osmolarity was 279.8 mOsm/L. Her ictal electroencephalogram (EEG) showed discharges of high amplitude spike-waves and multiple spikes-waves which localized to the right temporoparietal electrodes involving to the adjacent area. (Figure 1). The photoparoxysmal response was not observed during the photic stimulation. Brain magnetic resonance imaging (MRI) was normal. Functional MR and single photon emission computed tomography (SPECT) were not performed. Seizure control was achieved immediately after the glucose level fell to normal levels. When the blood glucose levels decreased slowly to about 150 mg/dL in five days, the seizures ended completely. No anticonvulsants were used. During the next 3 months follow-up, no seizures occured. The patient had been free of seizures with effective control of blood glucose.

DISCUSSION

Seizures are a rare but well recognized manifestation of severe hyperglycemia, particularly in non-ketotic hyperglycemic state (NKH). Focal epileptic seizure may be induced by non-ketotic hyperosmolar diabetic comas accompanied by severe hyperglycemia, hyperosmolality and dehydration with minimal or no ketoacidosis.[5] In this condition, focal motor seizures and epilepsy partialis continua (EPC) are the most common type, although generalized tonic-clonic seizures may also occur. Focal seizures have been reported in 19% of patients with NKH6 and focal seizures induced by eye movements have also been reported with NKH.[7]

The pathogenesis of focal seizures in NKH has not been completely understood. While focal seizures associated with NKH are refractory to antiepileptic drugs, they may be treated with adequate control of blood glucose. However, hyperglycemia alone is not an explanatory cause of seizures.[6,8,9] One of the suggested mechanisms is presence of a hyperosmolar gradient due to hyperglycemia between intracellular and extracellular neuronal compartments with subsequent dehydration, which may produce partial seizures.[10] The Krebs cycle is also inhibited in hyperglicemia.[11,12] This may cause an increase in gamma-aminobutyric acid (GABA) metabolism in the succinil semialdehyde pathway. Depressed brain GABA levels decreases the seizure threshold, decreasing the level of GABA, which is known to be an inhibitory neurotransmitter in the central nervous system. Due to depressed brain GABA levels, the seizure threshold decreases.

Reflex epilepsy refers to seizures that are regularly precipitated by a specific identifiable stimulus.[2] Based on the provocation mechanism, "reflex" seizure can be divided into a simple and a complex group.[13] Triggering factors include visual, auditory, somatosensory, mental, motor and others.[2,4,14] In the presence of a cortical lesion, hyperglycemia can facilitate an increase in frequency of focal motor seizures.[7,15] Localized tissue hypoxia may account for focal seizure activity in diabetics.[15] On the other hand, in cases with NKH, focal motor seizures related to posture have been reported, and it was suggested that proprioceptive-induced reflex seizures were related to unstable levels of blood glucose.[11,15,16] In these cases the seizures can result from active or passive movements of a limb, with or without any brain lesion.[11,15,16] In our case, there was no lesion on MRI.

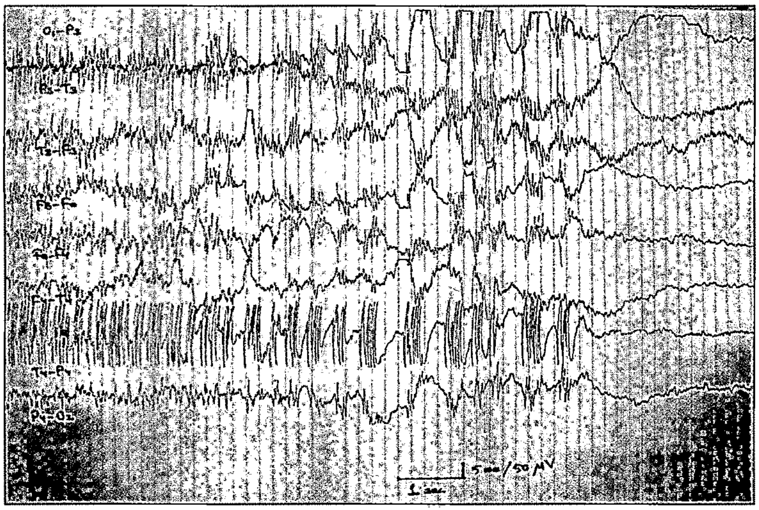

Figure 1. Discharges of high amplitude spike-waves and multiple spikes-waves which localized to the right temporoparietal electrodes and involved adjacent areas.

Various abnormalities in ictal EEG were reported in seizures with NKH. In some cases ictal EEG demonstrated periodic lateralized epileptiform discharges correlated with clonic contractions. In some, focal seizure discharge was recorded in the frontal, parieto-occipital or temporal region, and in the others no paroxysmal activity was recorded.[4,6,17] In our patient, ictal EEG showed ~~had~~ discharges of high amplituded spike-waves and multiple spikes-waves which localized to the right temporoparietal electrodes involving the adjacent area. Photoparoxysmal response was not observed during the photic stimulation.

Eye closure and closed-eyes tend to increase spontaneous EEG paroxysmal abnormalities. Previously, the effect of darkness and proprioceptive impulses on EEG abnormalities, which occur after closing of the eyes and disappear when the eyes are opened, were reported.[18] It was hypothesised that proprioceptive impulses generated by eye closure or the mechanisms associated with moving the eyes may trigger paroxysmal abnormalities.[18] In our case, a partial motor seizure was occurring at the eye circle during forced voluntary eye closure at the base of NKH. It may be related to increased GABA metabolism correlated to hyperglycemia without any ischemia. It was suggested that increased activity in reflex pathways might be secondary to the possibility of decreased GABA utilization in cortical and subcortical levels.[11,19] Seizures induced by forced eye closure are a rare but well-recognized form of reflex epilepsy. In our patient, these reflex focal seizures might be triggered by proprioceptive stimuli due to the pressure during strong closing of her eyes. Our patient had no photic sensitivity and, visual symptoms were not revealed by the patient during the seizure. Seizure control was achieved after she became normoglycemic and with adequate control of blood glucose, she continued to remain seizure free even by doing the movement, which previously induced the seizure. It is essential to improve metabolic deficiency for seizure control because seizures are generally refractory to anti-epileptic drugs and patients become seizure free with improvement of metabolic deficiency.

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case report

Experience with oral mexiletine in primary erythromelalgia in children

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Ann Saudi Med 2009; 29(4): 316-318

Primary erythromelalgia is characterized by burning pain, redness, and warmth in the extremities. We present two cases of primary erythromelalgia both of whom presented with a history of several months of severe burning pain in both hands and feet. Both patients had received multiple pain medications with no improvement in symptoms. Pain was relieved by putting affected parts in ice cold water, which resulted in immersion injury of the affected parts. Both patients stopped taking part in school and social activities. We tried oral mexiletine, a class Ib antiarrythmic agent, in view of its reported role in various chronic painful conditions. Dramatic improvement was observed with its use. Both patients improved after several weeks of use, and there were fewer soaking episodes. We observed no adverse effects with mexilitine therapy.

Erythromelalgia is a disorder characterized by severe burning pain, mainly involving the extremities and associated with erythema and increased temperature of the affected parts. Warmth aggravates the symptoms and cold provides relief.[1] Frequent immersion into ice cold water for relief of pain is a constant feature of the disease and is considered pathognomonic.[2] The pain associated with erythromelalgia is often resistant to treatment. Although a wide variety of therapies have been tried, no effective treatment is yet available. In a review of data for 168 patients with erythromelalgia at the Mayo clinic it was found that patients had used 84 different types of medications.[3] We present two patients with primary erythromelalgia, both of whom had received a number of painkillers before reporting to us. Both patients were given a trial of oral mexilitene and showed remarkable response.

CASE 1

A 12-year-old male presented to us with a history of severe burning pain in both hands and feet associated with redness and erythema for the previous 3 months. Pain was aggravated by heat and classically relieved by placing the hands and feet in ice cold water. Because of the severe pain, the patient would keep both hands and feet immersed in ice cold water most of the time, as a result of which the patient developed a severe immersion injury (Figure 1). There was no prior history of drug intake or immunization.

Clinical examination revealed a weight of 35 kg. There was no abnormality apart from the immersion injury and no neurological deficit. The complete blood count was normal apart from a hematocrit of 45%. RBC mass was 34 mL/kg. A complete metabolic workup, liver function tests, a work-up for connective tissue disorders (antinuclear antibodies, anti-double stranded DNA), coagulation tests, nerve conduction velocity (NCV), electromyography (EMG) were within normal limits.

Initially, the patient was given aspirin (15 mg/kg/day) for about 1 week with no improvement in symptoms. Subsequently, morphine (2.5 mg IV every 4 hours) was added, but again the patient showed no improvement. Treatment was discontinued after 2 weeks. The patient was started on oral mexiletine initially at 100 mg three times a day, which was increased subsequently to 200 mg three times a day. No adverse effect was observed. Improvement began after 2 weeks of therapy. The frequency, duration, and intensity of the pain episodes continued to decrease significantly and by 5 weeks of therapy all symptoms completely resolved. As of 6 months from discharge the patient had experienced very few episodes of mild burning pain, which did not incapacitate the patient. The patient reported no side effects from mexiletine therapy.

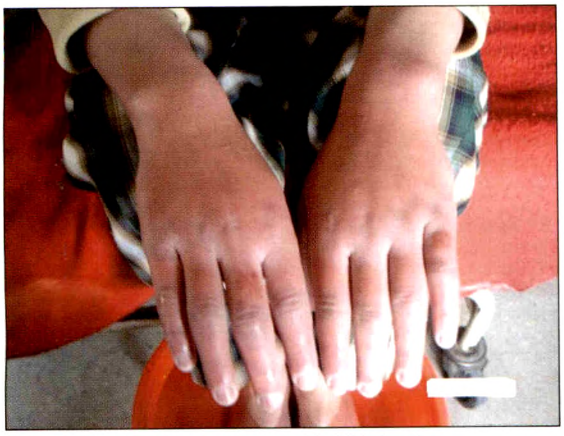

Figure 1. Photograph of a 12-year-old child showing erythromelalgia of both hands.

CASE 2

An 8-year-old male child presented with burning pain in both hands and feet associated with erythema for the previous month. Classically, the pain was relieved by immersing the affected part in cold water. Symptoms were aggravated by heat. The patient had developed immersion injury to both hands. There was no significant illnesses in the past prior to the disease. The patient was a product of a nonconsanguinous marriage with no family history of any myeloproliferative or connective tissue disorder. Clinical examination revealed a weight of 25 kg, and immersion injury of the left foot. A complete blood count revealed a hematocrit of 36%. A complete metabolic workup, liver function tests, workup for connective tissue disorders (antinuclear antibodies, anti-double stranded DNA), coagulation tests, nerve conduction velocity (NCV), electromyography (EMG) were within normal limits. Initially, the patient was treated with aspirin for about 1 week with no improvement. Subsequently, gabapentin was added. He showed a partial response to combination therapy, but the patient was still not able to participate in school and other social activities. He was started on oral mexiletine, initially 100 mg three times a day, which was increased subsequently to 200 mg three times a day. The frequency, duration, and intensity of the pain episodes continued to decrease significantly. During regular follow-up for two months after discharge the patient experienced no side effects from mexilitine and had marked improvement in symptoms with only a few episodes of pain, which were not incapacitating.

DISCUSSION

Because of lack of understanding of the pathophysiology and its low prevalence, treatment of erythromelalgia is poorly understood and often difficult to treat. Early studies suggested that aspirin effectively relieved symptoms, but aspirin appears to be significantly more effective when there is an associated thrombocythaemia and polycythemia vera.[2] Various pharmacologic trials have been conducted with varied results. These include use of tricyclic antidepressants, gabapentin, anticonvulsants, and others.[4,5] Mexiletine has been used in various chronic painful conditions and has been found quite effective.[6] It is a class IB orally active anti-arrhythmic agent, a sodium-channel inhibitor that shortens the action potential duration. Mutations in regions of chromosome 2q, which contain a cluster of sodium channel genes, have been identified among patients with primary erythromelalgia.[7] Sodium-channel blockers like mexiletine are widely used to treat neuropathic pain. Subacute or chronic inflammation also produces profound changes in the excitability of primary afferent neurons innervating the inflamed tissue.[8] Recent evidence suggests that post-translational modifications or abnormal expression of sodium channels in dorsal root ganglion neurons occurs after tissue inflammation.[9] In fact, there are few published case reports on the benificial effect of oral mexiletine in primary erythromelalgia.[10] Nathan et al[11] reported on an 11-year-old, white male child with primary erythromelalgia who demonstrated marked improvement following treatment with a combination of intravenous lidocaine and oral mexiletine therapy. Kuhnert et al[10] also demonstrated a similar effect in an adult patient with severe erythromelalgia. Mexiletine has also been found useful in inflammatory pain in experimental animals[12] and in the pain associated with diabetic neuropathy.[13] Mexiletine provides analgesia by blocking sodium channels at both peripheral and central sites. The ability of mexiletine to selectively block nerves in a more depolarized state makes this drug useful for blocking pain pathways in which neural activity is increased.

In summary, we present two cases of primary erythromelalgia who were suffering from a severe burning pain with a severe degree of immersion injury whose symptoms were signficantly controlled by oral mexiletine with no recognizable side effect of therapy.

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what's your diagnosis?

A 15-year-old girl with pancytopenia and congenital defects

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Accepted for publication April 2009

Ann Saudi Med 2009; 29(4): 319

A 15-year-old girl was referred to our hospital because of lethargy, palpitation and headache. Physical examination revealed a girl with short stature, café-au-lait spots, and left thumb abnormality. The hematologic parameters of the patient included hemoglobin 5.5 g/dL, WBC 2.96×10^9/L, platelets 38×10^9/L, and mean corpuscular volume 100 fL. Radiologic examination of the hands and abdomen revealed abnormal findings that gave a clue to the diagnosis.

1. What is the abnormal finding on this plain radiograph of the hands (Figure 1)?
2. What are the abnormal findings on this abdominal CT scan (Figure 2)?
3. What's your diagnosis?

FOR THE ANSWER, VISIT:

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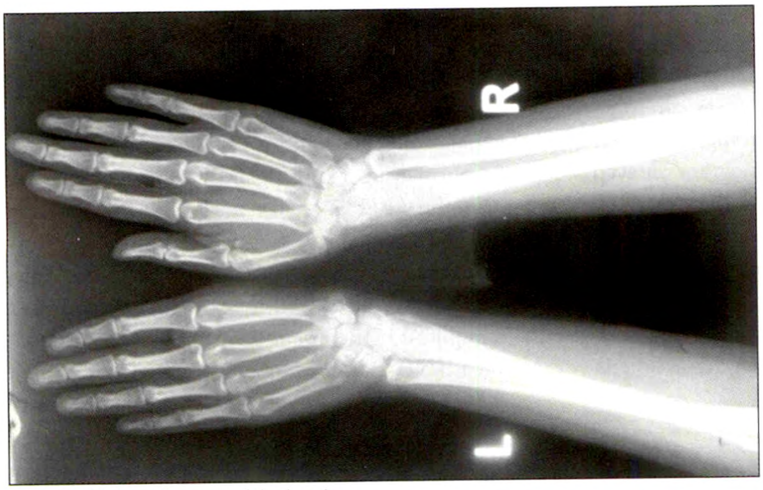

Figure 1. Plain radiograph of the hands.

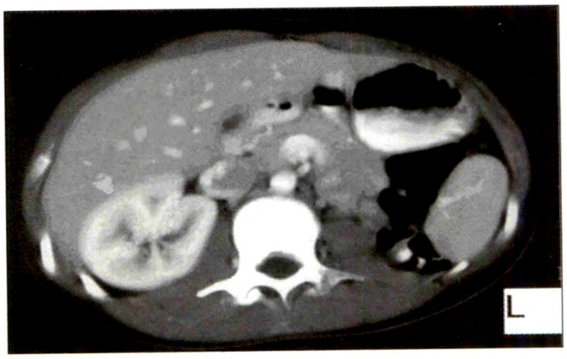

Figure 2. Abdominal CT scan.

Breast metastasis of small bowel carcinoid tumor misdiagnosed as primary breast cancer

To the Editor: Carcinoid tumors are rare, but constitute the most common gastrointestinal neuroendocrine tumors.[1] These tumors arise from enterochromaffin cells of the gastrointestinal tract. Carcinoid syndrome occurs in approximately 50% of patients with intestinal carcinoids and manifests as episodes of diarrhea, abdominal pain, and flushing.[2] Small intestinal carcinoids metastasizing to the breast have only sporadically been reported in the literature.[3] Metastatic breast carcinoid can be easily mistaken for primary breast carcinoma. This may potentially be detrimental for the patient, especially if the primary surgery is a mastectomy with axillary lymph node dissection.

A 64-year-old Caucasian female presented to her primary care physician with a chief complaint of left nipple pain. Mammogram showed a 2-cm solid mass in the lateral aspect of left breast suspicious for malignancy. Ultrasound-guided biopsy showed papillary carcinoma. Subsequently, a staging CT scan showed multiple hypodense lesions throughout the liver consistent with metastatic disease. Biopsy of the largest lesion confirmed the metastatic nature of the disease.

Diagnosis of stage IV papillary carcinoma of the breast was made and the patient was started on bevacizumab and paclitaxel. Following her initial treatment, the patient remained in good performance status except that she continued to complain of worsening diarrhea and facial flushing, which she had had for the last seven years prior to the current disease and which was attributed to menopause.

The persistent symptoms led the patient to seek a second opinion at the Yale Cancer Center. An octreotide scan showed multiple areas of increased activity within the liver, abnormal accumulation in the lower abdomen, upper pelvis, left midthorax and mid frontal and left superior parietal region of the calvarium (Figure 1).

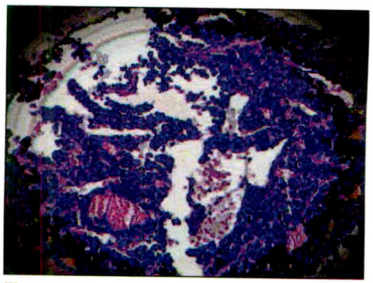

Figure 2. Breast biopsy of the patient showing a large nest of carcinoid tumor, infiltrating normal parenchyma (hematoxylin and eosin, ×40).

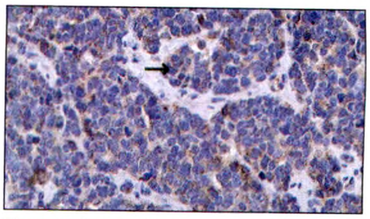

Figure 3. Breast biopsy of the patient showing immunoreactivity for chromogranin A.

Laboratory data showed increased pancreatic polypeptide (347 pg/mL; normal, up to 80 pg/mL) and serotonin (1448 ng/mL; normal, 101-283 ng/mL) levels. A previous breast biopsy was reviewed by the pathologist revealed a well-differentiated infiltrating neuroendocrine carcinoma (NET). Synaptophysin and chromogranin were intensely and diffusely positive confirming neuroendocrine differentiation (Figures 2, 3). Based on these findings, a diagnosis of NET of the small bowel was made with metastases to the liver and left breast. Lumpectomy of the breast was performed and chemotherapy was stopped. The patient has been treated with octreotide injection. Two years later, the patient is active and radiological imaging shows stable disease with no new areas of metastases.

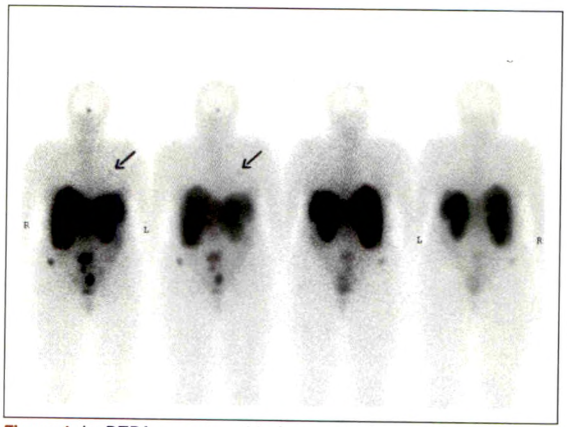

Figure 1. In-DTPA pentetreotide (octreotide) scan of the patient showing multiple areas of abnormal radiotracer activity within the abdomen, left breast (arrow), and calivarium.

Carcinoid tumors in the breast are rare. These tumors may occur as metastases from a known carcinoid tumor, or as a primary presentation of a metastatic carcinoid tumor, or as a primary breast tumor (Table 1).[4] Carcinoid tumors contain characteristic cytoplasmic granules that can be highlighted with special stains such as chromogranin, synaptophysin, or neuron-specific enolase.[5] Patients with carcinoid tumor metastatic to the breast should undergo lumpectomy alone, with multiple resections if more than one lesion

Table 1. Available data of reported cases with primary and metastatic carcinoid tumor to the breast.

	Average age, yr (range)	Unilateral/ bilateral	Location of primary	Misdiagnose as breast cancer before surgery	Carcinoid syndrome
History of carcinoid tumor (n=15)	54 (20-72)	11/1	Ileocecal, appendix, duodenum, pancreas, lung	6/15	4/15
Breast as first presentation (n=9)	56 (35-97)	8/1	Ileocecal, appendix, ovary	6/9	6/9
Primary breast carcinoid (n=38)	66 (35-97)	26/3	Breast	18/38	0/38

is present. Patients with primary breast carcinoid should be treated in a manner similar to invasive ductal breast cancer that is appropriate for the size and stage of the lesion.[6] It is important to differentiate between primary breast carcinoma, primary breast carcinoid tumor and metastatic disease to the breast because of differences in treatment.

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Left-sided Amyand hernia

To the Editor: Claudius Amyand, surgeon to King George II, was the first to describe in 1736 the presence of a perforated appendix within the hernial sac of an 11-year-old boy who had undergone successful appendectomy.[1] Since then, the presence of the appendix within an inguinal hernia has been referred to as "Amyand hernia", and still remains a rare occurrence. In this report we present a case of Amyand hernia in a 70-year-old man that differs from most other cases in that it was discovered at surgery for a left-sided inguinal hernia. After opening the hernia sac, the appendix and the cecum were found to be lying within it, with minimal adhesions to the sac (Figure 1). An appendectomy was done, the cecum freed of the flimsy adhesions to the sac, reduced within the abdominal cavity and a herniorrhaphy was performed. A hernia is defined as the protrusion of a viscus or part of a viscus through the walls of its containing cavity. It remains a commonly encountered condition in the inguinal region, where the hernial sac may contain the omentum or small bowel. Unusual contents may be encountered, such as the bladder, a Meckel's diverticulum (Littre hernia), or a portion of the wall of the intestine (Richter hernia). Although the last two mentioned are well-known even by their eponyms in standard textbooks and teaching practice, the Amyand hernia remains relatively unknown despite having been first reported nearly 170 years ago. The term Amyand hernia refers to the presence of the appendix within the hernia sac, and has been variously defined as the occurrence of either an inflamed or perforated appendix within an inguinal hernia, or simply, the presence of a non-inflammed appendix within an irreducible inguinal hernia.[1,2] The incidence of having a normal appendix within an inguinal hernial sac is about 1% whereas only 0.1% of all cases of appendicitis present in an inguinal hernia.[3] Most of the cases occur on the right side,[4] probably as a consequence of the normal anatomical position of the appendix, and also because right-sided inguinal hernias are more common than left-sided hernias. Although Amyand hernia has also been reported on the left side,[5] this is rare and may be associated with situs inversus, intestinal malrotation or a mobile cecum.[6] In our case, a mobile cecum was probably the cause of finding the appendix within the hernial sac on the left. Most of the reported cases present with underlying appendicitis, with the features of an obstructed or strangulated hernia. Perforation of the appendix within the sac may simulate perforation of the intestine within the hernia, and

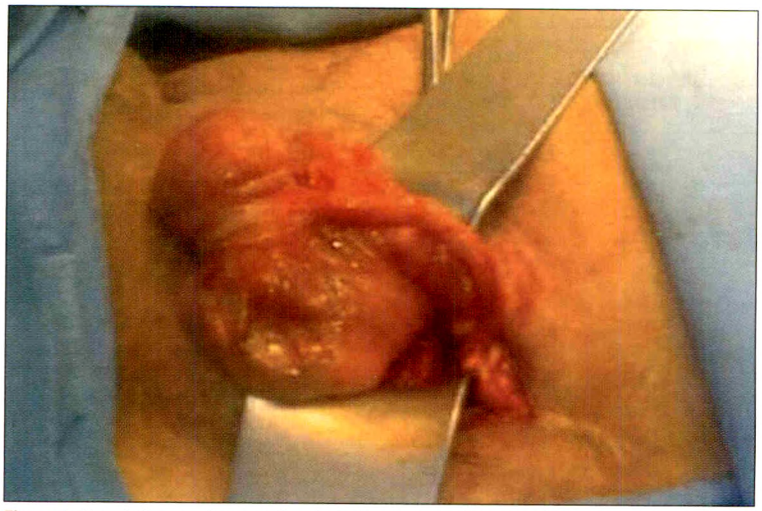

Figure 1. Non-inflammed appendix within the left sided inguinal hernial sac (Amyand's hernia).

it is rare to be able to make a clinical diagnosis of an Amyand hernia preoperatively. Although a preoperative CT of the abdomen may be helpful in reaching the correct diagnosis,[2] it is not a routine practice to perform a CT scan after diagnosis of an inguinal hernia. Also, our patient underwent an elective surgery for herniorrhaphy and did not have signs or symptoms in favor of a complicated inguinal hernia, so we were only able to make the diagnosis intraopertively. An important point is that if the base of the cecum is accessible through the hernial sac, it is easy to perform appendectomy but if it is not mobile enough, it is better to do it through a low midline laparatomy incision. Another issue is whether an appendectomy needs to be done. If the appendix is inflamed, appendectomy is mandatory, but if the appendix is normal in right-sided Amyand hernia, appendectomy is not recommended to avoid contamination of a clean hernia repair wound. In cases of left-sided Amyand hernia we suggest appendectomy even if the appendix is normal, because in these cases the cecum is mobile or the patient has situs inversus or intestinal malrotation.[6] Any future appendicitis will have an atypical clinical presentation. Amyand hernia must be kept in mind when a patient presents with a complicated or non-complicated inguinal hernia.

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RE: Serum viral markers in Iranian patients with congenital bleeding disorder

To The Editor: We have read with great interest the article of Dr Nassiri-Toosi in your journal[1] regarding the prevalence of hepatitis C infection in hemophilic patients. We disagree with the authors about the HCV prevalence rate in Iranian hemophilic patients. The Iranian Hemophilia Center resides in Emam Khomeini Hospital, which is a referral center for patients with liver disease, especially patients with viral hepatitis in Tehran. Most patients are referred to this center for evaluation of liver disease so their enrollment can lead to an overestimate of viral hepatitis prevalence in this type of patient. The hospital is a referral center for hemophiliac patients as well as hepatology and liver transplant patients. Many hemophiliac patients who attend this center have previously diagnosed liver disease. We made a similar mistake in 2001 (first report on HCV infection in hemophilia in Iran)[2] and reported a prevalence rate of 60.2% in a cross-sectional study in all hemophilic patients who attended to the "Iranian Hemophilia Society" between March 2000 and March 2001. After publication of the results, we found out that many of our subjects that were anti-HCV antibody positive were referred from other centers and the reported prevalence was overestimated. In a recent systematic review (in press) we determined that 40% of Iranian hemophilic patients are HCV infected. The high rate of nosocomial transmission of HCV infection as a result of a low standard of care might be another possibility that would justify the authors' findings.

The authors reported that genotype 1a (48.5%) was the predominant type and genotype 3a (33.3%) was common. Four patients were infected with type 1b (12.1%), one patient with type 2b (3%), and one patient with type 4b (3%). This finding is compatible with the opinion that the main source of HCV infection in Iranian hemophilic patients is from imported contaminated coagulation factor concentrates, and not the result of domestic transfusion (due to low 1b distribution, 1b is more common in polytransfused subjects).[3,4] However, we agree that HCV infection is the main cause of liver disease in this group of patients.

In the discussion about the comparison of the distribution of HCV genotypes in the studied population and other published data on the hemophiliac and non-hemophiliac populations in Iran, reference numbers 17 and 18 were also irrelevant to the HCV genotype distribution of Iran.

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Doppler ultrasonography in the diagnosis of Graves disease: a non-invasive, widely under-utilized diagnostic tool

To the Editor: We present the case of a patient with Graves disease (GD) to draw attention to the practical reliability of ultrasound (US) Doppler in the diagnosis of GD. We believe that this simple, non-expensive, non-invasive, and portable tool is under-utilized in the diagnosis of GD, and that most clinicians rely heavily on radioiodine (RAI) uptake scan for this purpose. Besides the radiation exposure encountered in RAI scintigraphy and the length and multi-phase application of the procedure, RAI scan is (roughly) 5-10 times more expensive than US. The diagnosis of GD can often be based solely on clinical grounds and simple blood tests, and without the need for imaging studies. The majority of such patients are first seen by their family doctors, and by the time a referral is made to an endocrinologist, both US and RAI scans are (often) already done. The problem is that even in the case where a US is ordered, no efforts are made to emphasize the characteristic intense Doppler flow in these cases; this pattern, referred to as "inferno", is almost pathognomonic for GD.[1-3]

A 28-year-old woman presented to the endocrine clinic with severe symptoms of hyperthyroidism of 2 months duration. She had no significant eye symptoms. On physical examination, she was found to have moderately severe hyperthyroidism, but she was clinically not in distress and was not in a thyroid storm. She had approximately 50 g symmetric firm goiter, with very loud bruits. Her thyroid function test showed thyroid stimulating hormone of <0.001 mIU/L; free T4 of 105.53 pmol/L; and total T3 >12.32 pmol/L. The patient brought an ultrasound image (Figure 1). As shown in the figure, the color Doppler depicts a high soft tissue vascularity, described as an "inferno". We believe that this particular feature of the US–"the inferno"–is under-utilized in clinical practice. It is anecdotally observed that a lot of physicians consider an RAI scan as the mainstay imaging study for hyperthyroidism, and often do not get US if GD is confirmed by the isotope scan. Even if US is ordered in the diagnostic work up of GD, we noted from cases referred for consultation that Doppler is not utilized. Furthermore, we noted that the literature is relatively scarce on the role of US in the diagnosis of GD.

Ralls and associates first used color Doppler sonography in 1988 for the diagnosis of GD.[1] They used the term "inferno" to refer to the pulsatile flow pattern in GD, which was obvious in all 16 patients with GD in their study, as compared to controls. Arslan and associates were able to demonstrate the peculiar diffuse hypervascularity in all 23 GD patients of their study.[2] Cappelli et al recently published a large prospective study[3] on hyperthyroid patients (n=1470, with 426 with GD), reporting excellent sensitivity and specificity of US in GD (by vascular Doppler pat-

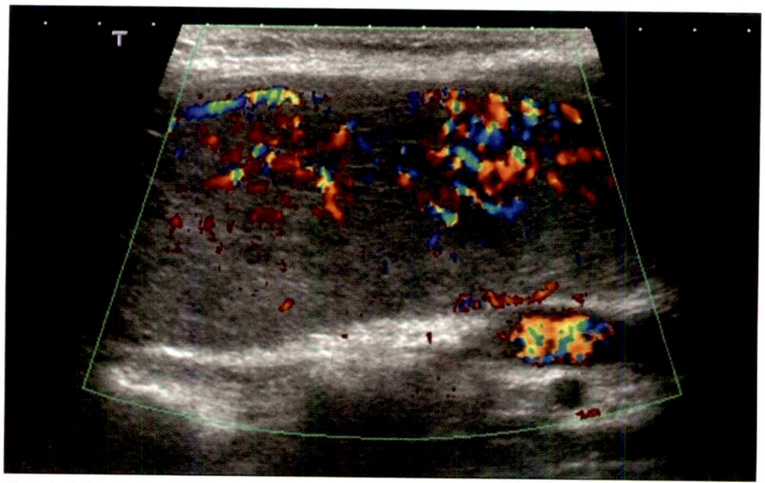

Figure 1. Ultrasound of the thyroid showing an intense vascularity on color Doppler that is consistent with an "inferno".

tern). The US Doppler had a 95% sensitivity and a 95% specificity, as compared to those of RAI scan (97% and 99%, respectively).

More recently, Kumar et al[4] reported the excellent diagnostic accuracy of peak systolic velocity of the inferior thyroid artery as measured by US Doppler in hyperthyroidism. In a study of 65 patients with hyperthyroidism (GD versus thyroiditis), this particular technique had a sensitivity of 96% and specificity of 95%, with a peak systolic velocity of 40 cm/sec as a cut-point diagnostic value. This technique has thus added a quantitative tool to supplement the qualitative tool of tissue vascularity; the two tools can be very helpful in the diagnosis of GD.

However, Levine cautioned[5] that cases of subacute thyroiditis would have any degree of vascularization (which would depend on the phase of the condition). Furthermore, no data are available on US findings in pregnant women with hyperemesis gravidara, which can be difficult to distinguish from GD in early pregnancy. Therefore, we believe that larger studies are warranted to evaluate the validity of US Doppler in the diagnosis of GD in pregnant women, especially in early gestation.

While GD can be often diagnosed with a certain degree of confidence by clinical evaluation and simple blood tests, some cases may be difficult to diagnose. This difficulty is especially encountered in the differentiation between GD and thyroiditis, and in particular in mild cases where pathognomonic features of GD, e.g. opthalmopathy, are absent. While RAI scan is the standard imaging study used in such situations, we believe that US may provide an alternative, especially when RAI scan is less available, less affordable (roughly $1500 vs $150, depending on geographical location), or contraindicated (e.g. pregnancy or lactation). However, clinicians should be aware of the occasional overlapping that may be encountered between GD and subacute thyroiditis.

It is prudent to point out that US should be considered in every patient with GD because incidental small thyroid cancers (<10 mm) could be missed by physical examination or RAI scans, as emphasized by Cappelli et al.[3] In this regard, clinical examination for the detection of thyroid nodules in general has a low sensitivity and specificity.[6-8] This is especially important in patients with goiters, such as in patients with GD where small nodules could be embedded within these goiters.[3]

We believe that radiology facilities should have an US protocol with Doppler patterns (color or power or both) in all patients referred for US, with a clinical diagnosis of GD, describing the pattern and whether it qualifies as an "inferno". Reporting radiologists should then emphasize this in their reports. Furthermore, Doppler peak systolic velocity of inferior thyroidal artery seems to be similarly promising in the diagnosis of GD.

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WHO EMRO Press

World Health Organization, Regional Office for the Eastern Mediterranean

Global status report on road safety

Nearly one half of all deaths on the road are pedestrians, cyclists and motorcyclists, new WHO report reveals

Egypt 17 June 2009

The first global assessment of road safety finds that almost half of the estimated 1.27 million people who die in road traffic crashes each year are pedestrians, motorcyclists and cyclists. While progress has been made towards protecting people in cars, the needs of these other vulnerable groups of users are not being met.

The Global status report on road safety provides the first worldwide analysis of how well countries are implementing effective road safety measures. These include limiting speed, reducing drink-driving and increasing the use of seatbelts, child restraints and motorcycle helmets. Funded by Bloomberg Philanthropies, the report presents information from 178 countries, accounting for over 98% of the world's population. It uses a standardized methodology that allows comparisons to be made between countries.

"We found that in many countries, the laws necessary to protect people are either not in place or are not comprehensive. And even when there is adequate legislation, most countries report that their enforcement is low," said WHO Director-General Dr. Margaret Chan. "We are not giving sufficient attention to the needs of pedestrians, cyclists and motorcyclists many of whom end up in clinics and hospitals. We must do better if we are to halt or reverse the rise in road traffic injuries, disability and deaths."

"In the Eastern Mediterranean Region...the findings of the Global status report on road safety are even more alarming when compared with the figures from 2002," said Dr. Hussein A. Geziary, WHO Regional Director for the Eastern Mediterranean. "They indicate that fatalities from road traffic injuries have witnessed a sharp rise in the past five years. The implications alert us to the urgent need for comprehensive and concerted actions to address the rising death toll."

"Traffic crashes are a leading cause of death, particularly among young people 5 to 44 years of age," said Mr Michael Bloomberg of Bloomberg Philanthropies. "For the first time, we have solid data to hold us accountable and to target our efforts. Road safety must be part of all transport planning efforts, particularly at this moment of focus on infrastructure improvements and road building by many countries around the globe."

While road traffic death rates in many high-income countries have stabilized or declined in recent decades, research suggests road deaths are increasing in most regions of the world and that if trends continue unabated, they will rise to an estimated 2.4 million a year by 2030. In addition, road crashes cause between 20 million and 50 million non-fatal injuries every year and are an important cause of disability. In many countries, support services for road traffic victims are inadequate. These avoidable injuries also overload already stretched health care systems in many countries.

The report found that underreporting of deaths occurs in many countries, and that few countries have completely reliable data on road traffic injuries. The highest death rates are seen in the Eastern Mediterranean and African regions, at 32.2 deaths per 100 000 population. This indicates a drastic rise in comparison to the 2002 data where the death rate in the Eastern Mediterranean Region stood at 26.4 deaths per 100000 population, and came second to the African Region.

"More than 90% of the world's road deaths occur in low-income and middle-income countries, while these countries only have 48% of the world's vehicles," said Dr. Etienne Krug, Director of WHO's Department of Violence and Injury Prevention and Disability. "Our roads are particularly unsafe for pedestrians, cyclists and motorcyclists who, without the protective shell of a car around them, are more vulnerable. These road users need to be given increased attention. Measures such as building sidewalks, raised crossings and separate lanes for two wheelers, reducing drink-driving and excessive speed, increasing the use of helmets and improving trauma care are some of the interventions that could save hundreds of thousands of lives every year."

The Global status report on road safety is currently being translated into Arabic to maximize its benefit in the Eastern Mediterranean Region. Meanwhile a regional report focusing on the situation of road safety in countries of the Region is being prepared and will follow in due time.

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Directory of Health, Medical Conferences and Professional Meetings in the Region

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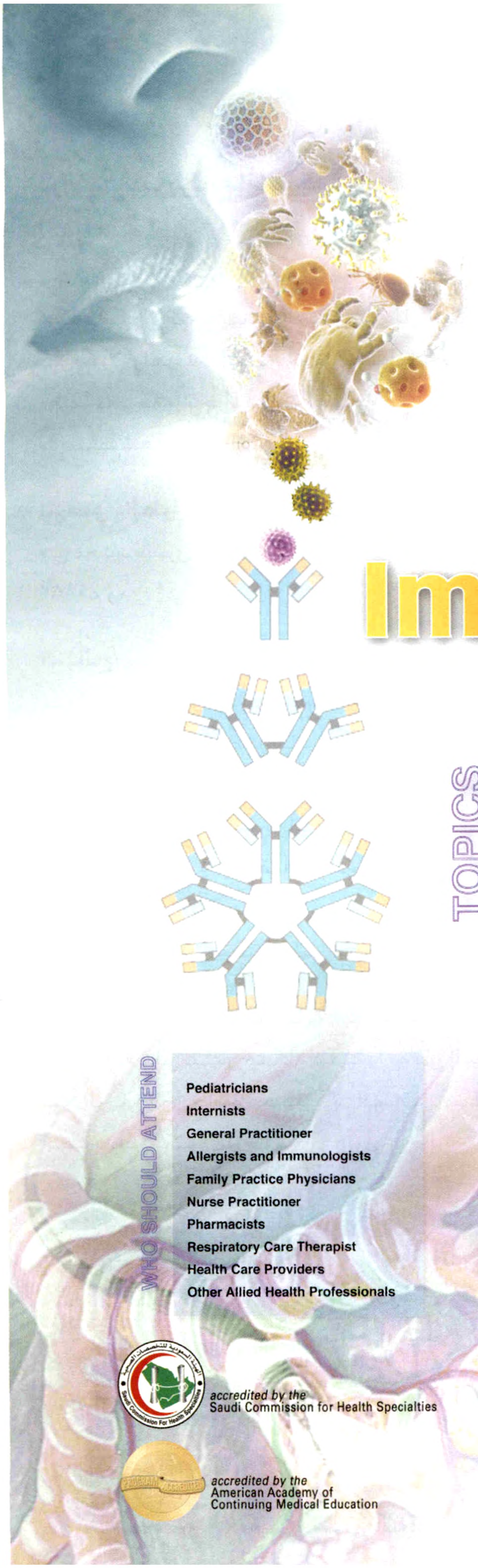

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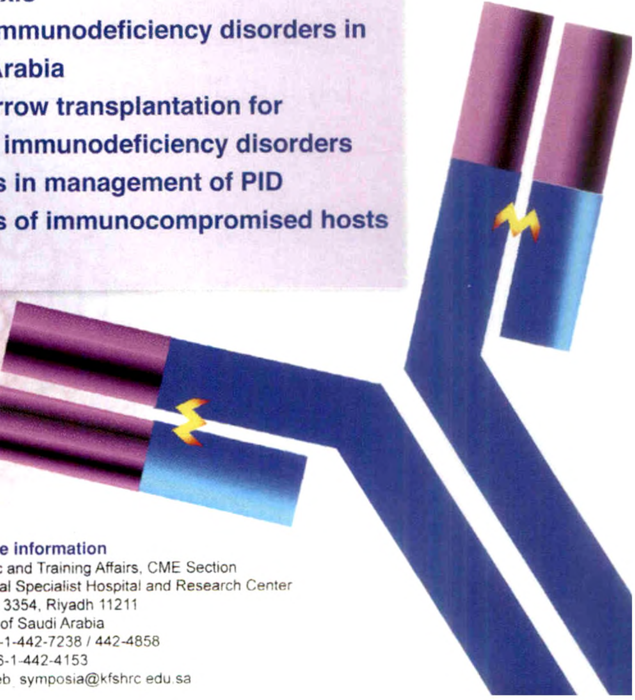

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دراسة سريرية باثالوجية لسرطان الثدي لدى الذكور: ٢٤ عاماً من الدراسة

مقدمة: نظراً لندرة إصابة الرجال بسرطان الثدي فإن عدد المرضى الذين أجريت عليهم الدراسة كان قليلاً. ولمعرفة المزيد عن أسبابه وعوامل خطرة وسماته السريرية والجينية والبثالوجية في دولتنا فقد قمنا بإجراء دراسة مراجعة على جميع الحالات التي قمنا بمعاينتها خلال العقود الأخيرة في مستشفانا.

المرضى والطرق: قمنا بتحديد كل حالة أصيبت بسرطان الثدي لدى الذكور في قاعدة البيانات في معهد شيري آي كشمير للعلوم الطبية في مدينة سريناجار بولاية كشمير في الهند بين ١٩٨٣م و٢٠٠٧م.

النتائج: وجدنا خلال ٢٤ عاماً ٣٢ حالة فقط مصابة بسرطان الثدي لدى الذكور. فقد ظهر سرطان الثدي لدى الذكور بنسبة ٢٫٨٪ من مجموع المرضى الذين تم استئصال أنسجة الثدي لديهم وشمل ذلك جميع آفات الثدي و٤٫١٪ من مجموع الحالات المصابة بسرطان الثدي. ومن بين ٣٢ حالة، أصيب ٢٠ منهم (٦٢٫٥٪) بعوامل الخطورة المرتبطة بالمرض. وأصيب ٩٣٫٧٪ بالسرطان القنوي الغازي. وكان لدى ثمانون بالمائة من المرضى إيجابية لمستقبلات الإستروجين. ووجدنا لدى ٧٠٪ منهم إيجابية لمستقبلات البروجستيرون. وكان لدى ٣٠٪ إفراط في هرمون (HER-2) ووجدنا إفراط هرمون (p53) بنسبة ٣٠٪ أيضاً. وقد لاحظنا وجود طفرة سرطان الثدي من النوع ٢ في ٤٠٪ من الحالات بينما لا يوجد مرضى مصابين بطفرة سرطان الثدي من النوع ١.

الاستنتاج: تشير نسبة إصابة ٤٫١٪ من الرجال بسرطان الثدي إلى أن المرض شائع في هذا الجزء من العالم على عكس ما كان معتقداً به في السابق. ويبدو أن سبب الإصابة بسرطان الثدي لدى الرجال هو إيجابية مستقبلات الهرمون، كما تشكل طفرة سرطان الثدي من النوع ٢ عامل خطورة واضحاً على الرجال.

دقة نظام فيشر للتسجيل ونظام بيانات تصوير الثدي في تحديد آفات الثدي الخبيثة بواسطة اختصاصيي الأشعة المبتدئين

الخلفية والأهداف: قام فيشر بتطوير نظام تسجيل في سنة ١٩٩٩م أدى إلى تسهيل التعرف على الآفات الخبيثة وتحديدها من قبل اختصاصي الأشعة المبتدئين. إن الهدف من هذه الدراسة هو تقييم جدوى هذا النظام في مساعدة المبتدئين على التشخيص الدقيق لآفات الثدي على صور الرنين المغنطيسي لتقييم العلاقة بين نظام بيانات تصوير الثدي بالرنين المغنطيسي (MRM BI-RADS) والتشخيص النهائي.

المرضى والطرق: قمنا بتقييم مورفولوجيا الآفات وحرائك تباين ٦٣ كتلة لدى ٤١ مريضاً على صورة الرنين المغنطيسي وأعطيناها تقييماً نهائياً على (MRM BI-RADS) ، باستخدام نظام فيشر للتسجيل. كما قمنا بتقييم الدقة بعد الحصول على التشخيص النهائي وصور المتابعة.

النتائج: كان هنالك ٢٥ آفة خبيثة و ٣٠ آفة حميدة. شوهدت ثمان (٨) آفات على صورة الرنين المغنطيسي فقط دون أن نتمكن من تحديد المرضيات لافتقارنا لمرافق الخزعة الموجهة بالرنين المغنطيسي في زمن الدراسة. على صورة تخطيط الثدي بالرنين المغنطيسي، صُنفت الآفات المسرطنة كفئة BI-RADS الخامسة لدى ١٦ حالة (٦٤٪) والرابعة لدى ٧ حالات (٢٨٪)، والثالثة لدى حالتين (١٠٪). وأما الآفات الحميدة فصنفت كما يلي: الفئة الخامسة لدى ٣ حالات (١٠٪)، والفئة الرابعة لدى ٦ حالات (٢٠٪)، والفئة الثالثة لدى ٣ حالات (١٠٪)، والفئة الثانية لدى ١٠ حالات (٣٣٪)، والفئة الأولى لدى ٨ حالات (٢٧٪). تنبأت فئة BI-RADS بدقة بآفات خبيثة بنسبة ٩٢٪ وآفات حميدة بنسبة ٧٠٪. وسبب التداخل بين سمات الآفات الالتهابية المزمنة والأورام السرطانية، على صورة الرنين المغنطيسي للثدي، إنخفاضاً في دقة تشخيص الآفات الحميدة مقارنة بالآفات الخبيثة.

الاستنتاج: إن الجمع بين MRM-BI-RADS باستخدام نظام فيشر للتسجيل يعتبر مفيداً وذات قيمة تكهنية مرتفعة خصوصاً لآفات الثدي الخبيثة كما أنه سهل التطبيق. إن التداخل في السمات بين الآفات الالتهابية الحميدة والآفات الخبيثة قد يؤثر على دقة تشخيص الأمراض الالتهابية.

نسب انتشار الأعراض النفسية لدى طالبات المدارس الثانوية السعوديات في مدينة أبها، بالمملكة العربية السعودية

مقدمة: يتسم سن المراهقة بحدوث تغيرات نفسية واجتماعية وإدراكية سريعة. الهدف من هذا البحث هو دراسة الصحة النفسية عند طالبات المدارس الثانوية السعوديات في مدينة أبها، بمنطقة عسير في المملكة العربية السعودية.

المرضى والطرق: أجريت دراسة بطريقة القطع المستعرض في عشرة (١٠) مدارس ثانوية للفتيات، باستخدام النسخة العربية المعدلة لقائمة الأعراض (٩٠) ٩٠ (SCL-revised -symptom ٩٠R) checklist وهو عبارة عن استبيان للصحة النفسية تم تطبيقه على الفتيات، من قبل طالبات الطب للسنة الرابعة.

النتائج: تمثلت الأعراض النفسية الأكثر شيوعاً لدى ٥٤٥ من الطالبات، في القلق الرهابي (١٦,٤٪)، الذهانية (١٤,٨٪)، القلق (١٤,٣٪)، الجسدنة (١٤,٢٪). وكانت نسب الإصابة بالاكتئاب، الأفكار الزورية والحساسية من الأشخاص، ١٣,٩٪، ١٣,٨٪، ١٣,٨ على التعاقب. وتمثلت الأعراض النفسية الأقل شيوعاً في العدائية (١٢,٨٪) والوسواس القهري (١٢,٣٪).

وبشكل عام وجدت الأعراض النفسية (من حيث شدة المعيار العالمي الإيجابي) في ١٦,٣٪ من الفتيات. أظهر تحليل التراجع اللوجستي المتعدد، عدم وجود علاقة ملحوظة بالعناصر الاجتماعية السكانية.

الاستنتاج: شيوع الأعراض والاضطرابات النفسية لدى طالبات المدارس الثانوية. و يتوجب على المهنيين الصحيين إدراك مشاكل الصحة النفسية عند الشباب والاهتمام بمعالجتها ومتابعة مثل هذه الحالات. ويحتاج الأمر إلى إجراء المزيد من البحوث لتحديد حجم المشكلة على المستوى المحلي.

عوامل الاضطرابات الجنسية لدى النساء الأردنيات والسلوك الجنسي لهن

مقدمة: تعرف الاضطرابات الجنسية لدى النساء بأنها مشاكل في الشهوة والإثارة والنشوة والألم الجنسي التي تؤدي إلى ضائقة نفسية أو صعوبات بين الأشخاص. وحيث أن دراسة النواحي الاجتماعية للاضطرابات الجنسية لدى النساء. لم يدرس سابقا بشكل جيد فإن والهدف من هذه الدراسة هي استكشاف النواحي الاجتماعية للاضطرابات الجنسية لدى النساء والسلوك الجنسي للنساء الأردنيات.

المرضى والطرق: تمت دراسة ستمائة وثلاث عشرة سيدة متزوجة في الفترة ما بين أكتوبر ٢٠٠٦م وأغسطس ٢٠٠٧م في المركز الوطني للسكري والغدد الصم والوراثة بعمّان، الأردن. أجرينا مقابلات للسيدات باستخدام استبيان خاص يناسب ثقافتنا مع ترجمة عربية لاستبيان منسب الوظيفة الجنسية لدى النساء (FSFI).

النتائج: ارتبط عامل التقدم في السن مع انخفاض المؤشر الإجمالي للاضطرابات الجنسية لدى النساء ونتائجها الميدانية. النساء اللاتي يعانين من البدانة هم أكثر عرضة لضعف الإثارة وضعف القدرة على الوصول إلى النشوة. أفاد ٥٨,٥٪ من النساء تقريباً بأنهن يهيئن أنفسهن إذا كانت لديهن رغبة جنسية، وأفاد ٦٨,٢٪ بأنهن يرتدين ملابس خاصة لهذا الغرض. وأفاد ٣٧,٢٪ من النساء فقط بأنهن من الممكن أن يطلبن من أزواجهن أموراً خاصة.

الاستنتاج: تعد الاضطرابات الجنسية مشكلة شائعة في الأردن. وقد تمت دراسة النواحي الاجتماعية ويجب أن تُجرى عنها المزيد من البحوث في المستقبل.

القياسات البشرية والبنية الجسدية لدى أطفال المدارس في البحرين

مقدمة: أجريت هذه الدراسة نظرا لقلة بيانات التقييم الشامل على المستوى الوطني حول القياسات البشرية والمشاكل الصحية المتعلقة بها لدى أطفال المدارس من سكان دولة البحرين في الفئة العمرية من ٦ إلى ١٨ عاما.

المرضى والطرق: تم إجراء دراسة مقطعية حول القياسات البشرية لدى أطفال المدارس ممن التحقوا بالمدارس الحكومية الابتدائية والمتوسطة والثانوية في جميع المناطق السكنية بدولة البحرين. شمل حجم عينة الدراسة ٢٥٩٤طالباً (١٣٢٦ إناث و١٢٦٨ ذكور) يمثلون ٢,٥٪ من عدد الطلاب الكلي. شملت القياسات البشرية الطول، الوزن، محيط منتصف الذراع وسمك ثنية الجلد في موقعين (العضلات الثلاثية و عضلات ما تحت الكتف). وقد تم استخدام بيانات مؤشرات القياسات البشرية من منسب كتلة الجسم وسطح عضلة الذراع. وقد تم استخدام معايير منظمة الصحة العالمية (٢٠٠٧م) ودراسة نتائج الفحوص الغذائية والصحية الوطنية كوسيلة مقارنة.

النتائج: مقارنة بمعايير منظمة الصحة العالمية، فإن متوسط الطول لدى أطفال المدارس والمراهقين من سكان دولة البحرين في الفئة العمرية من ٦ إلى ١٨ عاما كان قريبا من ٢٥٪ أو أقل، بينما كان متوسط منسب كتلة الجسم أثناء سنوات سن المراهقة مختلفاً لدى الذكور، لكن مرتفعاً عن معايير منظمة الصحة العالمية لدى الإناث، يصل إلى ٧٥ ٪. القيمة الحدية لمنسب كتلة الجسم لحالة السمنة/ البدانة المفرطة (كانت من ٨٥ إلى ٩٥٪) أعلى بمعدل ٣-٦ كيلوغرامات/متر مربع مقارنة بمعايير منظمة الصحة العالمية. بينما كانت نتيجة سمك ثنية الجلد أيضا أعلى مقارنة بنظرائهم من الأمريكيين. كانت عضلات الذراعين أقل بنسبة ملحوظة.

الاستنتاج: تشير نتائج الدراسة الحالية عن متوسط منسب كتلة الجسم وسمك ثنية الجلد إلى اتجاه متزايد نحو السمنة بين المراهقين والأطفال من البحرين ممن هم ضمن الفئة العمرية من ٦ إلى ١٨ عاما، خاصة لدى الفتيات، مما يعرض هذه الفئة العمرية إلى ارتفاع احتمال المعانة من بدانة البالغين والإصابة بعواقبها، وهناك حاجة ماسة لبرنامج تدخل طارئ.

انتشار إنزيم الكلبسيلة الرئوية المنتجة للبيتا لاكتاماز واسع الطيف والخاصية الجزيئية له بالرياض، السعودية

مقدمة: توجد تقارير قليلة في السعودية حول موضوع بيتا لاكتاماز واسع الطيف (ESBL) المنتجة من قبل الأمعائيات وخاصة إنزيم الكلبسيلة الرئوية. ولهذا، قمنا بتحديد مدى انتشار الكلبسيلة الرئوية المنتجة لإنزيم بيتا لاكتاماز واسع الطيف في الرياض وتمييز جين إنزيم بيتا لاكتاماز المسيطر في هذه المعزولات.

المرضى والطرق: تم عزل ٤٠٠ عينة من بكتيريا الكلبسيلة الرئوية من مستشفيين بالرياض خلال عام ٢٠٠٧م. وتم فحص إنتاجها لإنزيم بيتا لاكتاماز واسع الطيف (ESBL) باستخدام (ESBL-E-strips) وأساليب القرص المشترك. وقد تم استخدام فحص (PCR) للكشف عن جينات بيتا لاكتاماز (TEM)، و بيتا لاكتاماز (SHV) ، و بيتا لاكتاماز(CTX-M).

النتائج: تم تحديد نسبة مرتفعة من (ESBL) لـ ٥٥٪ من معزولات الكلبسيلة الرئوية. وقد كانت نتيجة فحص (PCR) للكلبسيلة الرئوية المنتجة لإنزيم بيتا لاكتاماز واسع الطيف ايجابية لجينات بيتا لاكتاماز (SHV,TEM,CTX-M) مع نسب انتشار بنسبة ٩٧,٣٪، ٨٤,١٪، و٣٤,١٪ على التوالي. تم العثور على جينات مشابهة في مجموعتين من الأنزيمات (CTX-M-١,CTX-M-٩) ضمن فصيلة (CTX-M)، مع انتشارات بنسبة ٦٠٪ و٤٠٪ على التوالي.

الاستنتاج: تؤكد هذه الدراسة وجود نسبة مرتفعة لإنزيم بيتا لاكتاماز واسع الطيف في المعزولات السريرية للكلبسيلة الرئوية في المستشفيات بالرياض. توضح هذه الدراسة الانتشار العالمي لجينات (bla CTX-M). إن هذا التقرير الأول على وجود جين (bla CTX-M) في المعزولات السريرية في السعودية إنما هو دليل على استمرار انتشار هذا الجين عالمياً.

المدونات الطبية السعودية

تصدر المدونات الطبية السعودية مرة كل شهرين عن مستشفى الملك فيصل التخصصي ومركز الأبحاث . ص.ب ٣٣٥٤ . الرياض ١١٢١١. المملكة العربية السعودية. يتم توزيع المدونات وإعداد الملخصات العربية بالتعاون مع د. زهير القاوي بواسطة موظفي إدارة الخدمات الإدارية بمستشفى الملك فيصل التخصّصي ومركز الأبحاث.

جميع المراسلات والاستفسارات وطلبات الاشتراك ترسل إلى المحرر الأول مكتب المطبوعات (ر.إ ٣٦).

سعر الاشتراك ١٠٠ ريال في السنة للأفراد داخل المملكة و٢٠٠ ريال في السنة للأفراد خارج المملكة و٥٠٠ ريال في السنة للمؤسسات. يمكن فتح اشتراك مجاني للأفراد و المؤسسات في الدول النامية.

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المدونات الطبية السعودية ر.إ (٣٦)
مستشفى الملك فيصل التخصّصي ومركز الأبحاث .
ص.ب ٣٣٥٤
الرياض ١١٢١١
المملكة العربية السعودية
هاتف: ٤٦٤٧٢٧٢-١-٩٦٦ تحويلة ٣١٨١٩/٣١٨١٥
فاكس: ٤٦٤٧٢٧٢-١-٩٦٦ تحويلة ٣١٨٧٥
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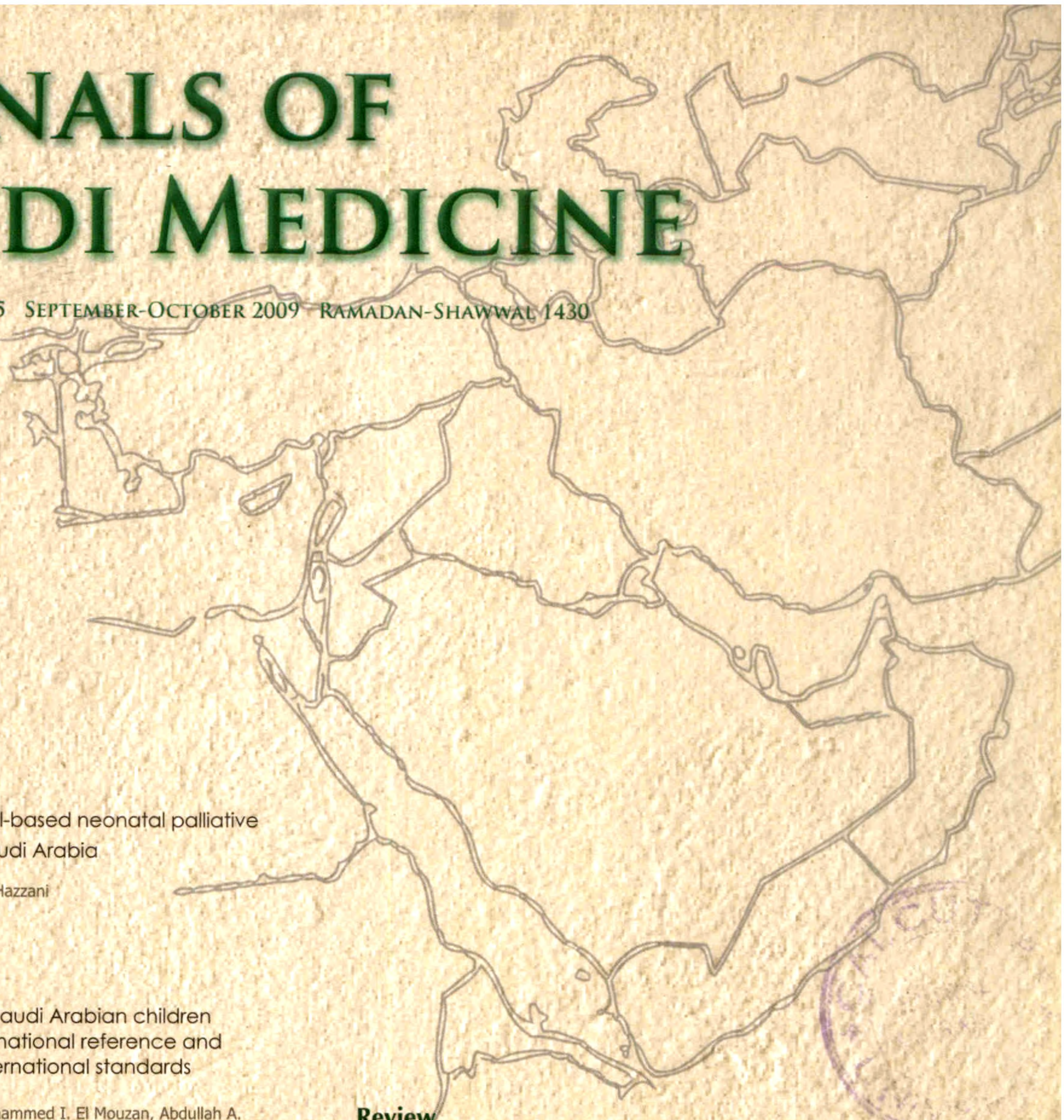
مجلة المدونات الطبية السعودية مفهرسة بواسطة الفهرس الطبي (المكتبة الوطنية للطب). والفهرس الطبي لمنظمة الصحة العالمية • إقليم شرق المتوسط. المحتويات الراهنة. التجارب الطبية. الوعي الراهن في العلوم الحيوية. الفهرس التراكمي للتمريض والعلوم الصحية المساعدة. الجمعية الأمريكية اللاتينية للمعلومات العلمية.
الرقم التسلسلي القياسي الدولي: ٠٢٥٦ - ٤٩٤٧
١٤٢٧-٠٤

ANNALS OF SAUDI MEDICINE

VOLUME 29 ISSUE 5 SEPTEMBER-OCTOBER 2009 RAMADAN-SHAWWAL 1430



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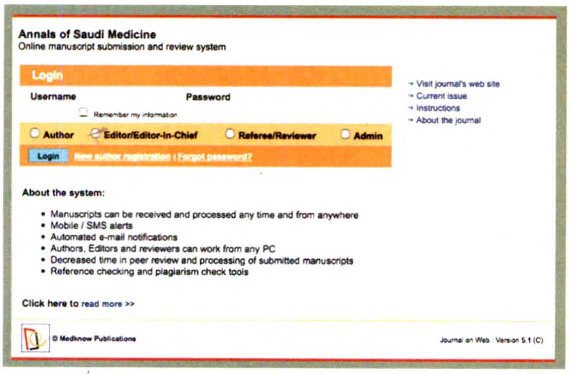

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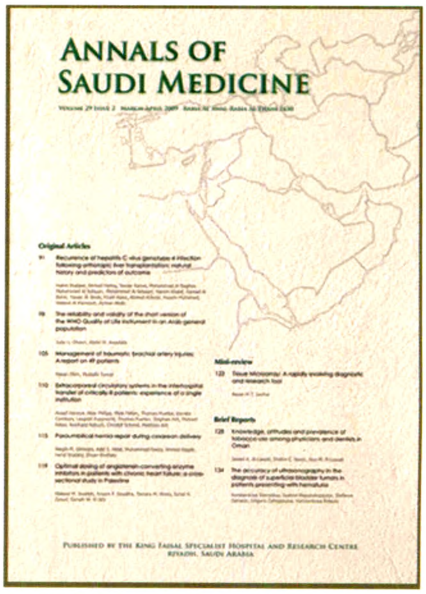

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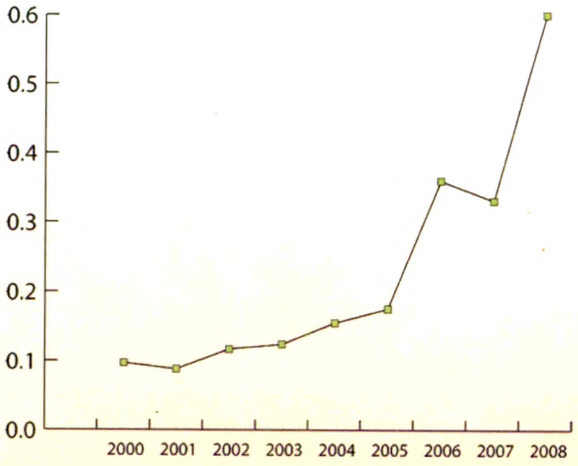

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Medknow Publications & Media Pvt. Ltd.,
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The *Annals of Saudi Medicine* is published bimonthly by King Faisal Specialist Hospital & Research Centre. Arabic abstracts are prepared, in association with Dr. M. Zuheir Al-Kawi, by the staff of the Office Services Department of King Faisal Specialist Hospital & Research Centre.

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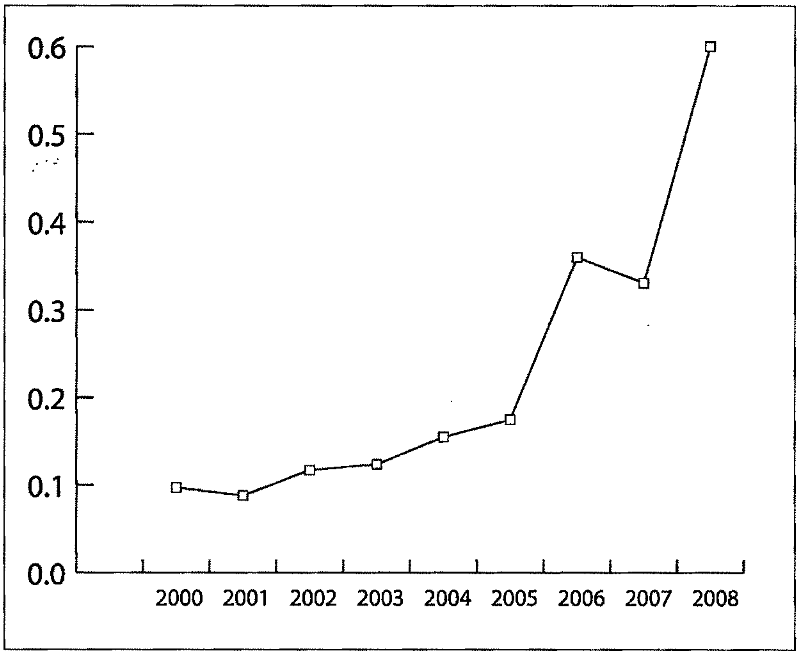

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SUMMARIES

PEDIATRICS

Body mass index in Saudi Arabian children and adolescents: a national reference and comparison with international data

Al Herbish and colleagues created reference body mass index (BMI) curves for Saudi children and adolescents using a stratified multistage probability sample of 35 275 subjects collected from the 13 health regions in Saudi Arabia. Four BMI curves were produced, from birth to 36 months and 2 to 19 years for girls and boys and compared with the WHO and CDC BMI charts. The curves are statistically representative values for Saudi children and adolescents.

Regional variations in the growth of Saudi children and adolescents

Using a cross-sectional representative sample of the Saudi population of healthy children and adolescents aged from birth to 19 years, El Mouzan and colleagues found significant differences in all growth parameters (weight for age, height for age, weight for age, stature for age, head circumference, body mass index) between regions, particularly between the southwestern and other regions. They conclude that regional variations need to be taken into consideration when assessing the growth of Saudi children and adolescents.

The prevalence of metabolic syndrome and cardiovascular risk factors in a group of obese Saudi children and adolescents: a hospital-based study

In 57 obese Saudi children and adolescents, Taha and colleagues found that 11 of 37 patients for which data was available met the criteria for metabolic syndrome. Of 39 who had a lipid profile, 10 had hypertriglyceridemia, 8 had hypercholesterolemia, 6 had elevated LDL cholesterol levels, and 6 had low HDL cholesterol levels. They note that Saudi children and adolescents have multiple risk factors associated with metabolic syndrome.

OPHTHALMOLOGY

Pediatric retinal detachment in the Eastern Province of Saudi Arabia: experience of a tertiary care hospital

In a retrospective review of 20 consecutive cases of pediatric rhegmatogenous retinal detachment (RRD) seen over a 3-year period, Cheema and colleagues found that trauma, myopia/vitreoretinal degeneration and prior ocular surgery were significant risk factors for RRD. Surgery was successful in 17/20 (85%) cases. Longer duration of RRD and macular involvement were associated with worse anatomical outcomes following surgery. The authors concluded that pediatric RRD is often associated with predisposing pathology.

ORAL HEALTH

Prevalence of oral lesions among Saudi dental patients

Al-Mobeeriek and AlDosari describe oral mucosal lesions found in 383 dental patients (15.0%) of 2552 patients seen over a 3-year period. The most commonly affected age group was 31 to 40 years of age, while the least affected were older than 61 years. The most common lesion was Fordyce granule, found in 98 patients (3.8% of all dental patients). The study provides data on 22 types of lesions seen in Saudi dental patients and provides a basis for future studies.

perspectives

The need for hospital-based neonatal palliative care programs in Saudi Arabia

Saleh Al-Alaiyan, Fahad Al-Hazzani

From the Department of Pediatrics, King Faisal Specialist Hospital and Research Center, Saudi Arabia

Correspondence: Saleh Al-Alaiyan, MD · Department of Pediatrics, MBC 58, King Faisal Specialist Hospital and Research Centre, PO Box 3354, Riyadh 11211, Saudi Arabia · T: +966-1-442-7761 F: +966-1-442-7784 · alaiyan@kfshrc.edu.sa · Accepted for publication July 2009

Ann Saudi Med 2009; 29(5): 337-341

The terms palliative care, supportive care, and comfort care are used to describe individualized care that can provide a dying person the best quality of life until the end. The term "end-of-life care" is also used in a general sense to refer to all aspects of care of a patient with a potentially fatal condition. While the concept of palliative care is not new, it has only recently been applied to the neonatal population. To the best of our knowledge, none of the neonatal intensive care units (NICUs) in Saudi Arabia have adopted a neonatal program for palliative care. We believe the main reason is lack of knowledge of such programs and the fear of being accused of being heartless and cruel by providing comfort care for dying babies. Comfort care begins with the diagnosis of a life-threatening/terminal condition, and continues throughout the course of illness regardless of the outcome. In this perspective, our aim is to introduce these programs for caregivers in the NICUs in Saudi Arabia. For this purpose, we have reviewed the current recommendations in establishing neonatal palliative care programs and discussed some of the social and religious aspects pertaining to this issue.

Advances in obstetric and neonatal care have led to increased survival in premature infants; however, it has been noted that a substantial rise in the postneonatal death rate had accompanied this decrease in neonatal mortality.[1] The need for palliative care in the neonatal intensive care unit (NICU) is accentuated by the high neonatal mortality rate when compared with mortality among older children. In the US, it has been calculated that 34% of childhood deaths occur in the neonatal period as per the report of the Institute of Medicine (2003); When Children Die: Improving Palliative and End-of-Life Care for Children and Their Families.[2] They also reported the five leading causes of infant death. These, in descending order, were: (1) congenital malformations, deformations, and chromosomal abnormalities, which accounted for one-fifth of all infant deaths; (2) short gestation and low birthweight; (3) sudden infant death syndrome (SIDS); (4) newborns affected by maternal complications of pregnancy; and (5) newborns affected by complications of placenta, cord, and membranes. These leading causes differ from one country to another. In a report that included 193 countries, the major causes of neonatal death globally were: infections (sepsis/pneumonia, tetanus, and diarrhea) (35%); preterm birth (28%); and asphyxia (23%).[3]

In the Asir region, Saudi Arabia, the major causes of neonatal mortality were low birth weight (45%), congenital malformations (30.8%), infection (13.6%), and birth asphyxia (7.7%).[4] A recent single center report from Saudi Arabia involving 79 871 live births and 526 deaths showed that prematurity and its complications were the initial causes of neonatal and postnatal deaths (42%), followed by lethal malformations (36%), and hypoxic ischemic encephalopathy (5%), while 17% of cases died of different disorders.[5]

Hence, dealing with the death of an infant in the NICU is a relatively common problem. Most neonatal deaths occur during the first week of life, so it is mostly the NICU staff confronted with the palliative care of dying neonates. Clinical experience shows that many aspects of care in palliative situations are not well known to the healthcare providers. Its impact on staff can be large, but its impact on families can be immeasurable with lifelong implications. One goal of comfort/palliative and end-of-life care is to minimize avoidable conflicts related to poor communication, cultural misunderstandings, deficient clinical care, and approaches to decision making that fail to assure families that they and the healthcare team are doing their best for the child. Such failures can haunt family members and clinicians long after a child's death.

Therefore, understanding the right process of palliative care by the NICU personnel has a positive impact on families. When such measures are the focus of care, everyone in the NICU stands to benefit, including the newborn patient, his or her family, and the NICU staff. We would like to outline the main pillars of neonatal palliative care and to look at the potentials and the barriers especially to culture sensitivity and spiritual support, when such programs are established at our hospitals.

What is palliative care?

In the year 2000, the World Health Organization (WHO)[6] defined palliative care as an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual. Additionally, the Health Resources and Services Administration (HRSA) has set forth the following working definition: Palliative care is patient- and family-centered care. Palliative care is meant to optimize the quality of life by active anticipation, prevention, and treatment of suffering. It emphasizes use of an interdisciplinary team approach throughout the continum of illness, placing critical importance on the building of respectful and trusting relationships. In newborns, it is holistic and extensive care for an infant who is not going to recover. The care should include pain and symptomatic management, psychosocial support for family members, spiritual support for family members, and attention to the newborn's quality of life and best interests as determined through a culturally sensitive, negotiated, family-centered approach.[7-9]

Intravenous access should be kept in place to provide medication for symptom relief. These infants may be suffering from pain, seizure activity or respiratory distress. Doses of medication (that include narcotic and nonnarcotic analgesics, sedatives, hypnotics, and anticonvulsives) should be adequate to relieve these symptoms. The doses can be obtained from neonatal medications books with the help of the local pharmacist.[10]

Who is eligible for comfort care?

The categories of newborns listed below are provided for educational purposes and can be taken as examples by the local institutions to add more eligible infants with different clinical pathologies.[11]

Newborns at the limit of viability,[12] with extremely low birth weights and gestational ages, if no growth restriction exists. Recently, the General Presidency of Scholarly Research and Ifta, Saudi Arabia issued a legal opinion (fatwa # 231) on March 6 2008, regarding premature infants born less than six lunar months which is equal to 177 days, i.e., 25 week's gestation and two days. The legal opinion clearly stated that *"in case of infants born less than six lunar months, two specialized physicians could study the infant clinical condition and based on their opinion the infant can be offered full resuscitation if it is beneficial to the infant or to leave him/her without intervention to die but should not be deprived from nutrition or fluid".*

Newborns with multiple congenital anomalies incompatible with prolonged life, such as trisomy 13, 15, or 18, triploidy, thanatophoric dwarfism, Potter syndrome/renal agenesis and severe lung hypoplasia, anencephaly, holoprosencephaly, inoperable heart anomalies, some cases of hypoplastic left heart syndrome, severe congenital diaphragmatic hernia with hypoplastic lungs; inoperable conjoined twins.

Newborns not responding who are deteriorating despite providing all appropriate efforts such as nonresponsiveness to aggressive resuscitation, severe cases of brain injury, such as hemorrhages or leukomalacia, severe asphyxia, and multiple end-organ failure.

Case studies

The following cases may help to demonstrate who is eligible for palliative care:

Case 1

Baby A was a male born at 24 weeks' gestation with a birth weight of 600 g. Apgar scores were low due to chorioamnionitis and placental abruption. He developed severe respiratory distress and metabolic acidosis that required mechanical ventilation, surfactant therapy, and volume expanders. Soon after NICU admission, he developed seizure activity that required an anticonvulsant, which became almost continuous and refractory to three anticonvulsants. Brain imaging showed bilateral grade IV intraventricular hemorrhage with evidence of periventricular leukomalacia. The baby continued to have seizures most of the time for more than two weeks. Further, he developed episodes of severe bradycardia and irregular breathing while he was on low ventilatory support. Several meetings were held with his parents by the NICU staff and the pediatric neurologist. A decision was made to make him a No Cardiopulmonary Resuscitation (CPR) with comfort measures. His ventilatory settings weaned gradually while sedation increased and he died shortly thereafter.

Case 2

Baby B was a full-term, male, born with hypoplastic left heart syndrome that was diagnosed in utero. During pregnancy, the parents were prepared and educated about the disease and its outcome. At birth, the pediatric cardiologists found the cardiac anomalies were inoperable and cardiac transplantation was not even considered because of lack of any experience for this age group at our hospital. Several meetings were held with the family and a decision was made to make him a No CPR and he was discharged home on diuretics. There was a follow-up with the family who reported his death peacefully at two months of age.

Cultural sensitivity and spiritual support

Caring for patients across cultures requires additional skills in the areas of cultural sensitivity, awareness, knowledge and competency. Furthermore, sensitivity is a key to successful interactions between providers, patients, and families. Listening and attentiveness, combined with background knowledge, gives dignity and respect to others, a natural expression of competence.

In Saudi Arabia, Islam is the main religion; however, many caregivers are non-Muslims and may be non-Arabs. For these non-Muslims, they need to understand that Islam holds life as sacred and belonging to God and Muslims believe, as many other religions, death is only a transition between two different lives. Sacred texts and traditions, particularly the Qur'an and the Sunna "the example of the Prophet Muhammad" are the primary sources for a shared spiritual or religious response to illness among Muslims. The Qur'an repeatedly states that life is an examination. It makes no pretence that the trials and tribulations that life has to offer are significant and, at times, extremely difficult to bear; we are also reminded that these tribulations are in all cases surmountable.[13] "*Of a surety we will test you with something of fear and hunger, loss of life...but give glad tidings to those who patiently persevere*" Qur'an 2:155-57.

Muslim parents will not accept scientific explanations on the probability of living as the only factor involved in a medical decision. Parents need to be reminded of Allah's Will, and physicians are only helping, but the ultimate outcome is in the hands of Allah. Lack of trust in physicians or hospitals and the fear of committing sins may be the reasons for parents not to accept the medical decisions, but are willing to transfer authority for such decisions to professionals or religious scholars who they trust and believe that they do the best for their baby. Furthermore, they need to be reminded that Islam assures that the destiny of their children is Paradise. "*And they who believe and whose seed follow them in faith, We cause their seed to join them (there), and We deprive them of nought of their (life's) work. Every man is a pledge for that which he hath earned*" Qur'an 52:524. This destiny is given to them as a way of honoring them for the patience they show upon losing these little ones. It is also a sign of the magnificent and the all-embracing mercy of Allah that covers everything and everyone. They should be reminded to pray more frequently that Allah alleviates the sufferings of their dying children because Allah increases the rewards of parents who show patience in face of tribulations.

When a Muslim dies, ideally, the face of the person who has died should be turned towards Makkah, but in hospital turning the face towards the right should be sufficient. The arms and legs should be straightened and the mouth and eyes closed and the body covered with a sheet. A baby dying at or even before birth has to have a name. The corpse is ritually bathed before burial. A stillborn baby can be dealt with in the same manner as a live birth. Following the child's death, there are religious, social and bereavement rituals that are explained in detail by al-Shahri and al-Khenaizan.[14,15] The bereavement care should include not only the parents but also siblings, grandparents, other relatives, friends, nurses, physicians, and other staff members who have cared for the child.

Strategy for developing a palliative care program

Development should focus on the concept that palliative care is a part of the continuum of care, including parent choice and integrity throughout. The lack of continuity of care during the stages of death and dying with newborns is the first issue to be raised by professionals in order to discuss the need for a multidisciplinary palliative care team to effect continuity of care through to end-of-life.[16] Furthermore, a comprehensive approach to palliative care for seriously ill neonates, which would begin well before the neonate is imminently dying, should be integrated with other treatment modalities earlier in the disease course. One of the major defects in care is inadequate communication by the staff with parents and other members of the family. Thus, education of healthcare professionals in palliative care and instituting the model will accomplish the goals of the program. This can be achieved by developing educational tools and guidelines for the palliative care program, which could be obtained from the experiences of others in this field.[17] There are seven stages in the launch and a quality run in the development of a neonatal palliative care program. These are: building the case for a hospital-based palliative care program, designing an operational plan, presenting the business plan, implementing palliative care services, measuring program quality and impact, marketing the palliative care program and sustaining and growing the program.

The program should include well-experienced nurses who play clinical leadership roles on the palliative care team, as well as neonatologists, program administrators, educators, and researchers.[18] Once the program is implemented, it should be evaluated in 6-month increments and the input of parents should be taken into consideration. Outcome measures can be used to assess deficiences and determine necessary changes to be corrected by the team.

Barriers to neonatal palliative care

Despite the existence of a universal protocol in palliative care for dying babies and their families, provision of this type of care remains ad hoc in contemporary neonatal settings. Several barriers have been reported and they vary from one place to another. The input of nurses looking after dying neonates was the main source for identifying most of these barriers. Several themes emerged from the literature indicating that barriers for neonatal nurses may be attitudinal, clinical, educational, institutional, regulatory, and financial. Australian NICU nurses identified the following barriers: (1) inadequate staffing to support palliative care practice; (2) a physical environment that is not conducive to palliative care practice; and (3) technological imperatives and parental demands.[19]

The Neonatal Palliative Care Attitude Scale (NPCAS) surveys the following key barriers: (a) neonatal death viewed as a failure; (b) adjustment from a curative to palliative care approach; (c) difficult communication with parents of dying neonates; (d) previous and traumatic exposure to neonatal death; (e) conflicts among providers around end-of-life decision making; (f) NICU environment; (g) lack of support for nurses providing end-of-life care; and (h) lack of formal training for nurses.[11] Solving these barriers in a timely manner will maintain the continuation of the program.

Conclusion

Establishing neonatal palliative care programs at our hospitals is one of the vital needs in our institutions. These programs will provide crucial support for parents in going smoothly through their stressful events with a feeling that they are not abandoned. Speaking to parents about palliative care is not an easy task. Parents need to hear that physicians are willing to continue to provide the best medical care possible for their infants. They need to know that this continuing care will include frequent assessments by care givers and social workers in addition to adjusting medications so that their infant is comfortable. It is important to offer the ability to have a second opinion and an ethics or religious consultation. The language used should be lay person language to clarify medical terms, and the terms "withdrawal of treatment" or "withdrawal of care" should be avoided. It is also important not to give them the feeling that they are responsible for the infant's death, but they should understand that they cannot change the situation and the only thing can be offered is to support the infant's short-life with comfort and dignity.

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Body mass index in Saudi Arabian children and adolescents: a national reference and comparison with international standards

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Ann Saudi Med 2009; 29(5): 342-347

BACKGROUND AND OBJECTIVES: Because there are no reference standards for body mass index (BMI) in Saudi children, we established BMI reference percentiles for normal Saudi Arabian children and adolescents and compared them with international standards.

SUBJECTS AND METHODS: Data from a stratified multistage probability sample were collected from the 13 health regions in Saudi Arabia, as part of a nationwide health profile survey of Saudi Arabian children and adolescents conducted to establish normal physical growth references. Selected households were visited by a trained team. Weight and length/height were measured and recorded following the WHO recommended procedures using the same equipment, which were subjected to both calibration and intra/interobserver variations.

RESULTS: Survey of 11 874 eligible households yielded 35 275 full-term and healthy children and adolescents who were subjected to anthropometric measurements. Four BMI curves were produced, from birth to 36 months and 2 to 19 years for girls and boys. The 3rd, 5th, 10th, 25th, 50th, 75th, 85th, 90th, 95th, and 97th percentiles were produced and compared with the WHO and CDC BMI charts. In the higher percentiles, the Saudi children differed from Western counterparts, indicating that Saudi children have equal or higher BMIs.

CONCLUSION: The BMI curves reflect statistically representative BMI values for Saudi Arabian children and adolescents.

Body mass index (BMI), also known as the Quetelet or Kaup Index, is derived from the equation: Body weight in kilograms divided by length or height in squared meters.[1,2] It is a useful index for measurement of optimal physical growth in children. BMI norms are well established in the World Health Organization (WHO) and the Center for Disease Control (CDC) growth curves.[3,4] These norms have also been established in various countries showing an important ethnic and secular trend effect.[5] Several attempts have been made to establish BMI curves for Saudi children and adolescents but none were thorough and representative.[6-9] In this study, we present reference BMI curves for normal Saudi children and adolescents and compare it to the WHO and the CDC curves.

SUBJECTS AND METHODS

A nationwide project to establish normal anthropometric measures for Saudi Arabian children and adolescents was approved and granted by King Abdulaziz City for Science and Technology (KACST), Riyadh, Saudi Arabia. The project was then implemented by cooperative work between the College of Medicine, King Saud University and the Ministry of Health, Riyadh, Saudi Arabia. The guidelines and criteria of Waterlow et al for such projects were followed.[10] These guidelines require that measurements be done on a well-nourished healthy population, that the sample should include 200 individuals in each age and sex group, the study should be cross-sectional, the sampling procedure should be defined and reproducible, and the measurement should be carefully made and recorded by observers trained in anthropometric techniques using a well-tested design and calibrated equipment at frequent intervals. Sample selection was based on the most recent population census at the start of the study with the assistance of the general directorate of statistics, Ministry of Planning in Saudi Arabia.[11]

Taking an average and perhaps a conservative Saudi family size of 3 children, 14 000 households will theoretically yield a sample size of 42 000 children and adolescents (0-19 years of age). This was enough to produce a valid and representative result with a standard error of less than 5%. Households were randomly selected using a stratified multistage probability sampling procedure. The details of the selected households (location, name of the family head, and other information) were provided by the above mentioned general directorate of statistics.[11] As an important prerequisite for this project, a pilot study was performed in Buraidah City targeting 70 households. This succeeded in testing the procedure starting from training teams to locating the households to collection of the data. Minor modifications were done in the procedure and some difficulties and unexpected obstacles were overcome. The questionnaire in its final version contained three major parts: first, the demographic data of all family members and their medical history; second, physical examination; and third, the measurements after assuring eligibility criteria comprised the following: Saudi family with children and/or adolescents, born at term and free of chronic illnesses based on the history and the physical examination.

At least two investigators actively participated in training the teams in the 13 health directorate all over Saudi Arabia. These investigators remained in constant communication with the team heads to solve any unexpected difficulties. Furthermore, they were responsible for reviewing all completed questionnaires sent to the project headquarters in Riyadh before data entry was initiated. The techniques of measurement were done as per WHO recommendations.[12] This included measuring the child's length (for <2 years old) with two observers with the child in supine position on a flat surface stadiometer with a fixed head and sliding feet ends, or standing height (for >2 years old) performed by one observer following the recommended standards. Length and height measurement was recorded to the nearest 0.1 cm. The weight was performed with minimal clothing and recorded to the nearest 0.1 kg. The equipment was standardized in that two to three new sets were purchased specifically for the project per directorate. This equipment was easily calibrated, repaired, carried, and moved around. Reliability and accuracy was further assured by following the intra- and inter-observer variations done randomly in 1% of the sample. This was randomly performed on the 1st and the 15th household, respectively, by doing the measurement twice. All data were double-checked, multiple frequency tables were scrutinized, and statistical techniques were used to detect deficiencies and inaccuracies. The date were entered utilizing Epi info 2002 CDC, US, software program published by the CDC.[13] Birth date which was recorded from the birth certificate or the Saudi national identification card was converted from Hegira to Gregorian and the decimal age was calculated. A published software was used. The lambda, mu, sigma (LMS) method proposed by Cole and Green was utilized for curve construction, smoothing of weight and height and the calculated BMI [wt (kg)÷(L or Ht m^2)] against age for both boys and girls.[14]

RESULTS

Of the 14 000 targeted households, 11 874 (84.8%) were found eligible as the remaining were either vacant or occupied by families who were non-Saudis or had non-eligible children. However, this number of households yielded 35 279 eligible full-term and healthy children and adolescents for measurements. The sample was well distributed per region indicat-

Table 1. Distribution of eligible children and adolescents for measurements.

Region	Eligible children no. (%)
Makkah Al Mokarramah	6430 (18.1)
Riyadh	6395 (18.0)
Eastern Province	3810 (11.1)
Aseer	3459 (9.9)
Al Jouf	2347 (6.6)
Najran	2241 (6.3)
Al Madina Al Monawarah	2123 (6.0)
Northern Borders	2044 (5.8)
Hail	1945 95.5)
Gizan	1613 (4.7)
Qassim	1293 (3.7)
Al Baha	864 (2.5)
Tabuk	715 (2.0)
TOTAL	35,279 (100)

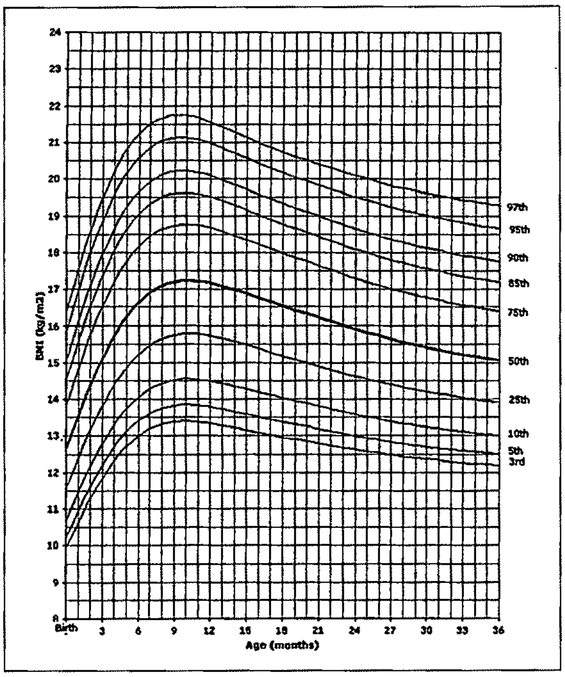

Figure 1. BMI for age-percentiles: girls, birth to 36 months.

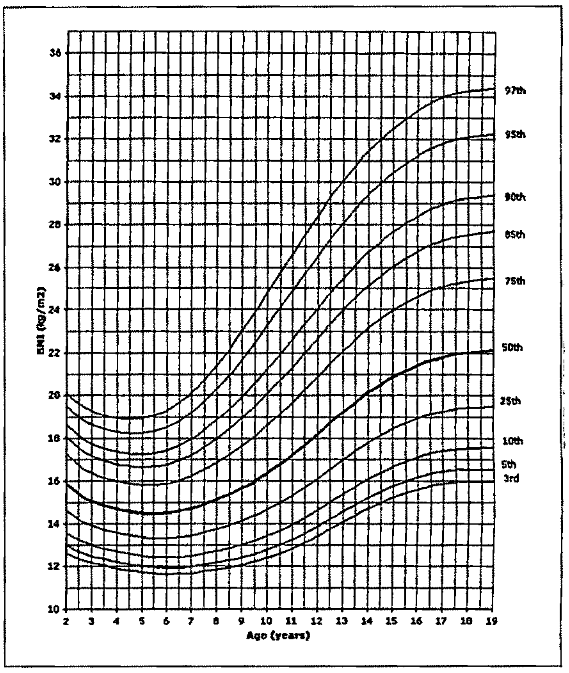

Figure 2. BMI for age-percentiles: girls, 2 to 19 years.

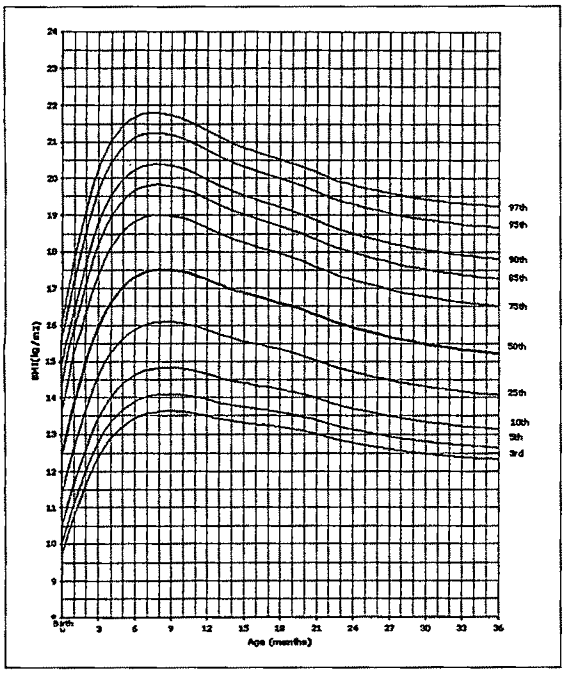

Figure 3. BMI for age-percentiles: boys, birth to 36 months 43×55 mm.

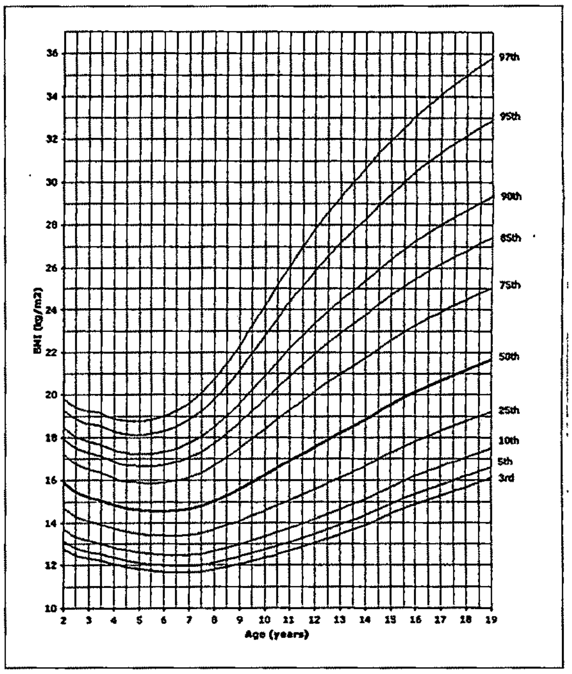

Figure 4. BMI for age-percentiles: boys, 2 to 19 years 43×55 mm.

ing good representation (Table 1). The female to male ratio was almost equal (49.5% were females and 50.6% males). Four BMI curves were created: 0-36 month and 2-19 years for both females and males. Ten percentiles were formed similar to the CDC 2000 growth curves. These were the 3rd, 5th, 10th, 25th, 50th, 75th, 85th, 90th, 95th, and 97th percentile. The 85th percentile was included for its important value as a cut-off point for definition of overweight. These curves are shown in Figures 1, 2, 3, and 4. In

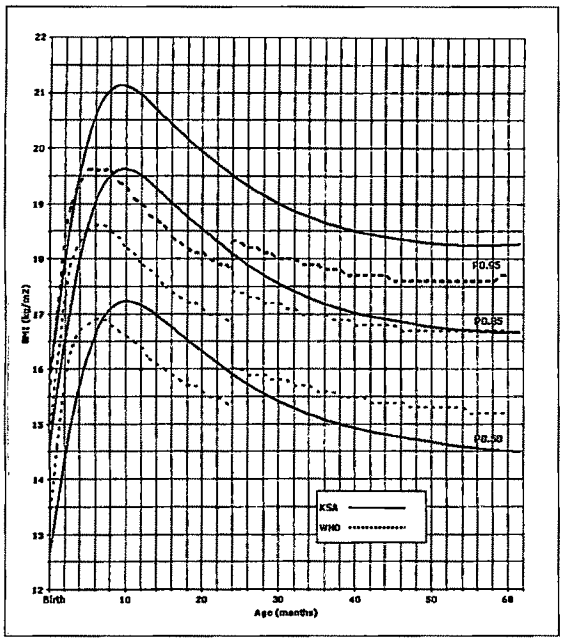

Figure 5. BMI for girls from birth to 60 months: comparison with WHO.

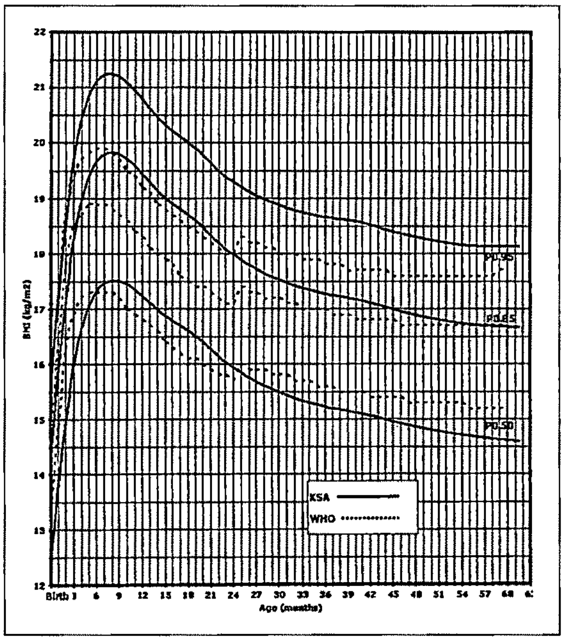

Figure 6. BMI for boys from birth to 60 months: comparison with WHO.

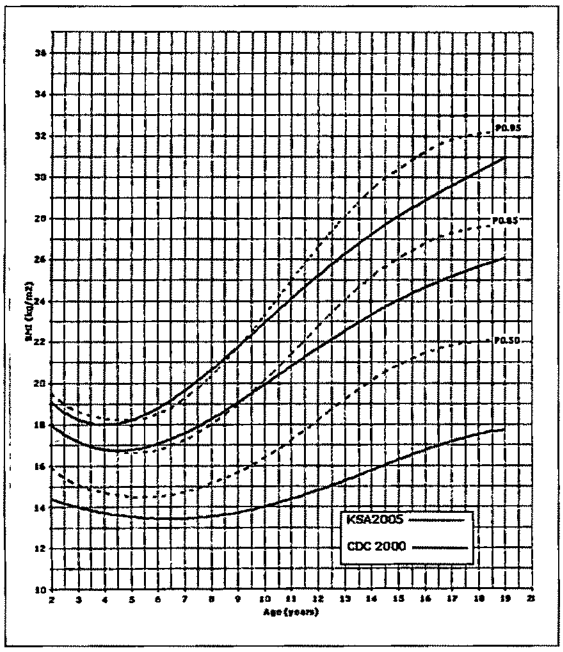

Figure 7. BMI for girls from age 2 to 19 years: comparison with CDC.

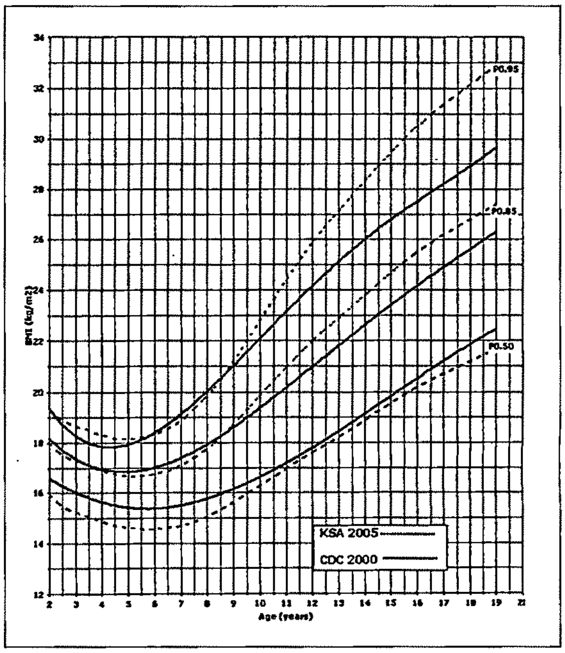

Figure 8. BMI for boys from age 2 to 19 years: comparison with CDC.

an attempt to make a comparison between the present study curves and other internationally available curves, we overlapped the present curves with the WHO and the CDC 2000 available curves for the 0-60 months and the 2-19 years of age, respectively (Figures 5, 6, 7, and 8).

DISCUSSION

Establishing norms for every community has become a necessity. Growth charts for Saudi children and adolescents have finally been established for use in the assessment of both healthy and diseased children.[15] An important parameter of growth is BMI. This has been useful in the assessment of physical growth in children and in the definition of obesity, both in children and adults.[16] Furthermore, BMI has been found to correlate very well with other long-term health parameters, e.g. blood pressure.[9,17] Among the various tools to assess overweight and obesity, BMI has therefore become more frequently used during the last few decades. BMI is affected by ethnicity.[5] It is therefore necessary to establish BMI for children and adolescents for the Saudi community where obesity has become prevalent in both children and adults.[18-20] This is due perhaps to changes in the lifestyle of the Saudi community. Weight and BMI have shown a continuous increase over the decades.[5,18] Al Hazzaa demonstrated rising trends in BMI, body fatness, central obesity, and prevalence of obesity among Saudi school boys over the last two decades.[18,21]

In establishing any normal value, it is very pertinent to compare these values to what is available internationally. In this study, we have overlapped the calculated BMI for the children and adolescents included in the study with the available WHO (young) and the CDC (old) BMIs. It is very interesting to note that higher percentiles show a difference, illustrating that Saudi children may be equal or even more in BMI compared to their western counterparts. This coincides with the fact that BMIs over the last two decades have been increasing.[21] This phenomena have also been noticed in other communities such as the US and Australia and some neighboring countries (such as Kuwait and Bahrain).[5,22,23] The sex differences noted in the present study depict that female children and adolescents may have higher BMI values compared to males is in line with the reports of Al Shehri et al.[20] The lower percentiles, however, were less than the WHO and CDC counterparts, particularly beyond six months of age.

We believe that the present study is quite representative for Saudi children and adolescents as it has followed a multi-stage probability random sampling procedure, which is known to be the strongest design to select a representative sample of any population. Furthermore, the methodology of case finding, accurate equipment, and accurate measurements with strong intra- and interobserver variation observations further augment the strength of the representation. Therefore, we highly recommend that these BMI curves be used for reference purposes for Saudi children and adolescents and perhaps for other neighboring countries. These curves should be referred to for assessment of healthy children and children suffering from chronic illness in order to monitor normal growth, an important goal for a proper long-term care and management. Children with specific disorders such as chromosomal anomalies should have their own curves. This has fortunately been established for some children such as Saudi children with trisomy 21.[24]

Acknowledgment

The authors would like to thank the teams who participated in the field work, and Cecile Singson Sael and Pia Miguel for typing the manuscript.

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original article

Regional variations in the growth of Saudi children and adolescents

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Ann Saudi Med 2009; 29(5): 348-356

BACKGROUND AND OBJECTIVES: No previous study has provided a detailed description of regional variations of growth within the various regions of Saudi Arabia. Thus, we sought to demonstrate differences in growth of children and adolescents in different regions.

SUBJECTS AND METHODS: The 2005 Saudi reference was based on a cross-sectional representative sample of the Saudi population of healthy children and adolescents from birth to 18 years of age. Body measurements of the length, stature, weight, head circumference and calculation of the BMI were performed according to standard recommendations. Percentile construction and smoothing were performed using the LMS (lambda, mu and sigma) methodology, followed by transformation of all individual measurements into standard deviation scores. Factors such as weight for age, height for age, weight for height, and head circumference for children from birth to 3 years, stature for age, head circumference and body mass index for children between 2-18 years of age were assessed. Subsequently, variations in growth between the three main regions in the north, southwest, and center of Saudi Arabia were calculated, with the Bonferroni: method used to assess the significance of differences between regions.

RESULTS: There were significant differences in growth between regions that varied according to age, gender, growth parameter and region. The highest variation was found between children and adolescents of the southwestern region and those of the other two regions The regression lines for all growth parameters in children <3 years of age were significantly different from one region to another reaching – 0.65 standard deviation scores for the southwestern regions (*P*=.001). However, the difference between the northern and central regions were not significant for the head circumference and for weight for length. For older children and adolescents a significant difference was found in all parameters except between the northern and central regions in BMI in girls and head circumference in boys. Finally, the difference in head circumference of girls between southwestern and northern regions was not significant. Such variation affected all growth parameters for both boys and girls.

CONCLUSION: Regional variations in growth need to be taken into consideration when assessing the growth of Saudi children and adolescents.

Growth indicators in the form of weight, length, stature, head circumference, weight for length and body mass index (BMI) for age are important tools for the assessment of growth of children and adolescents. Variations in growth are well known between countries as well as within the same country.[1,2] In Saudi Arabia, previous studies based on the growth of children and adolescents have been conducted and comparisons with other countries have been made.[3-7] However, to our knowledge, none of these studies provided a detailed description of regional variations of growth within Saudi Arabia. In this report, we analyze regional variations in the most recent and comprehensive growth study in Saudi children and adolescents.[8]

SUBJECTS AND METHODS

The design and methodology of the Saudi reference, which is the basis of this analysis of regional variations, have been reported in detail elsewhere.[8] Briefly, standard guidelines and criteria were followed in the determination of the sample size.[9] The study sample was selected by a multistage probability sampling procedure from a stratified listing based on the population census available at the time of the study. Accordingly, the sample was a representation of all the socioeconomic strata. The majority of young children were on both breast milk and formula feedings. A pilot study was designed to test all components of the project before data collection. A training workshop was conducted for the members of the field teams in each of the 13 regions of Saudi Arabia. Data collection was made by house-to-house visits where a survey questionnaire, clinical examination and body measurements were completed by primary care physicians and nurses.

The lambda, mu and sigma (LMS), statistical methodology was used to construct and smooth the growth charts.[10-12] Growth data collected from three regions from the north (Hail Jouf, Northern Borders) were compared with data collected from two regions from the southwest (Gizan and Aseer) and with two regions in the middle of the country (Riyadh and Qassim). The final LMS model was used to transform all individual measurements into standard deviation scores (SDS). Three steps were performed: In the first step, a separate cubic regression curve, where the response ("*y*-variable") is the SDS and the covariate ("*x*-variable") is age, was fitted to the data in each of the three categories of regions. These regression lines describe how the mean SDS of a given measurement changes with age in each region. The fit of the three cubic regression curves was then compared with the fit of three quadratic regression curves. If the difference in fits was not statistically significant, then the quadratic models were accepted and they were then compared with three linear regression curves and so on until the simplest model that might be fitted was three different horizontal lines. The three final regression lines were then plotted to provide a graphical description of the differences between regions. The second step was to statistically test the fit of the model involving three separate regression lines with the fit of the model based on a single common regression line. The standard F test was used to determine the statistical significance of the fit of the above-mentioned models and if the *P* value was small (less than .05, or less than .01 if the sample size was large); there were significant differences in how the mean SDS of a given measurement of a given age group and a given sex change with age. The third step, after a finding a significant difference, the same methodology was used to compare the difference between pairs of regions in turn to see whether they are significantly different from each other. To account for carrying out multiple comparisons between pairs of regions for a particular measure, the Bonferroni method which divides the total significance level into three (i.e., .01/3), was used. Accordingly, the difference between pairs of regions would be significant if the *P* value was less than .003.

RESULTS

Number of children and adolescents

The number of children and adolescents used in the analysis was 7723 (3912 boys and 3811 girls), 5072 (2590 boys and 2482 girls) and 6336 (3209 boys and 3127 girls) from the central, southwestern and northern regions, respectively. The number of children from 0 to 3 years were 4331, 1653, 2099 and those between 2 to 18 years were 3525, 3413, 4174 in the central, southwestern and northern regions, respectively. The difference between the total number of children and the sum of the two age groups is caused by the overlap 2-3-year age group.

General interpretation

The reference line for the average of the three regions is indicated on the figures as "all". The units are standard deviation scores based on all of the data used to fit the LMS model for a given measurement in order to examine the nature of the differences of that measurement over the age range. The figures clearly highlight the differences between the regions over the age range. Where there is no significant difference between pairs of regions (for example north-central), the curves are fairly close, but for pairs of regions that are significantly different they are well separated. The *P* values in this analysis indicate whether or not there are overall significant differences of a given parameter between regions. For example, in Figure 1a, it is clear that the regression line of the *z* score of weight for boys aged birth to 3 years in the southwest was negative relative not only to the curves of the central and north, but also to the curve of "all" regions which is the reference line, indicating a lower weight than any other region, reaching a *z* score of – .65 below the regression line. On the other hand, the regression line for weight of children in the north and central regions are all positive relative to the reference line reflecting better weight of children living in these regions. The same method of interpretation applies to all figures.

Table 1. Significance levels of regional variations, 0-3 years.

Parameter	*P* values for boys		
	North-Central	Southwest-Central	Southwest-North
Weight	.001	.001	.001
Length	.001	.001	.001
Weight for length	.003	.001	.001
Head circumference	.004	.001	.001
Parameter	***P* values for girls**		
	North-Central	**Southwest-Central**	**Southwest-North**
Weight	.001	.001	.001
Length	.001	.001	.001
Weight for length	.071	.001	.001
Head circumference	.139	.001	.001

Number of children: 4331 in central, 1653 in southwestern, and 2099 in the northern region.

Table 2. Significance levels of regional variations, 2-18 years.

Parameter	*P* values for boys		
	North- Central	Southwest-Central	Southwest-North
Weight	.001	.001	.001
Stature	.001	.001	.001
Head circumference	.005	.001	.001
Body mass index	.001	.001	.001
Parameter	***P* values for girls**		
	North- Central	**Southwest-Central**	**Southwest-North**
Weight	.001	.001	.001
Stature	.001	.001	.001
Head circumference	.001	.001	.015
Body mass index	.272	.001	.001

Number of children: 3525 in central, 3413 in southwestern, and 4174 in the northern region.

Birth to 3-years old

Comparison of the weight for age *z* scores between regions in the age group between birth and 3 years is depicted in Figure 1a for boys and Figure 1b for girls indicating a significant difference between all three regions (P=.001). The pattern of regional variation in the length for age z scores in the age group between 0 and 3 years is presented in Figure 2a for boys and Figure 2b for girls which show again a significant difference between all three regions (P=.001). Figures 3a and 3b illustrate the variation of the head circumference in the birth to 3 year age group for boys and girls, respectively, indicating no significant difference between north and central (P=.004 for boys and .139 for girls), but a significant difference between north and southwest and central and southwest (P=.001). Regional variations in weight for length in the birth to 3 year age group are shown in Figure 4a for boys and Figure 4b for girls with a clearly significant difference between all three regions for boys. For girls, however, the difference was not significant between north and central (P=.071), but was significant between north and southwest and central and southwest (P=.001).

Two to 18-years old

In older children and adolescents from 2 to 18 years of age, comparison of the weight for age z scores is presented in Figure 5a for boys and Figure 5b for girls which shows a significant difference between all three regions (P=.001). Regarding stature for age, regional variation is shown in Figure 6a for boys and Figure 6b for girls, again showing statistically significant differences between all regions (P=.001). Figures 7a and 7b illustrate the pattern of regional variation of head circumference for age in boys and girls respectively. For boys, there was no significant difference between north and central (P=.005), but the difference was significant between north and southwest and central and southwest (P=.001). For girls, however the regional variations in head circumference was significant between north and central (P=.001) and central and southwest (P=.001), but not significant between north and southwest (P=.015). The pattern of variation in *body mass index for age* is shown in Figure 8a for boys and Figure 8b for girls. The difference was significant for boys between all three regions (P=.001), but not significant for girls between north and southwest (P=.272). Tables 1 and 2 show the details of significance of difference between pairs of regions for the age groups birth to 3 and 2 to 18 years, respectively.

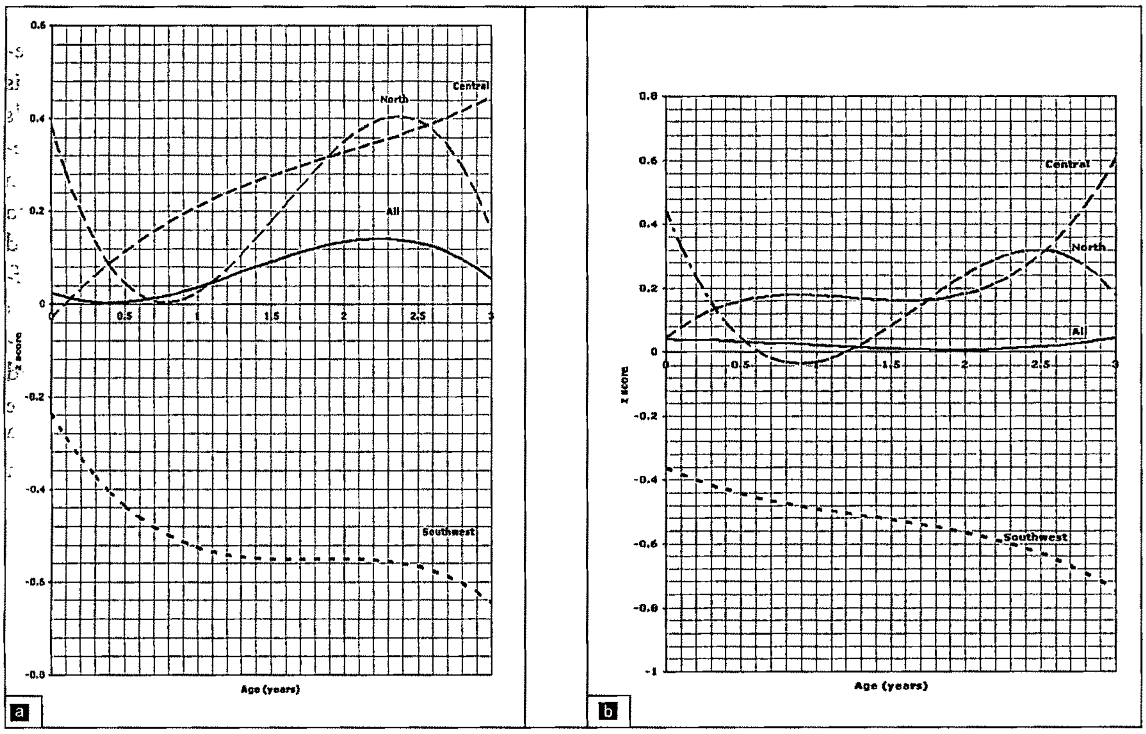

Figure 1. Weight of children aged 0 to 3 years, 1a for boys, 1b for girls.

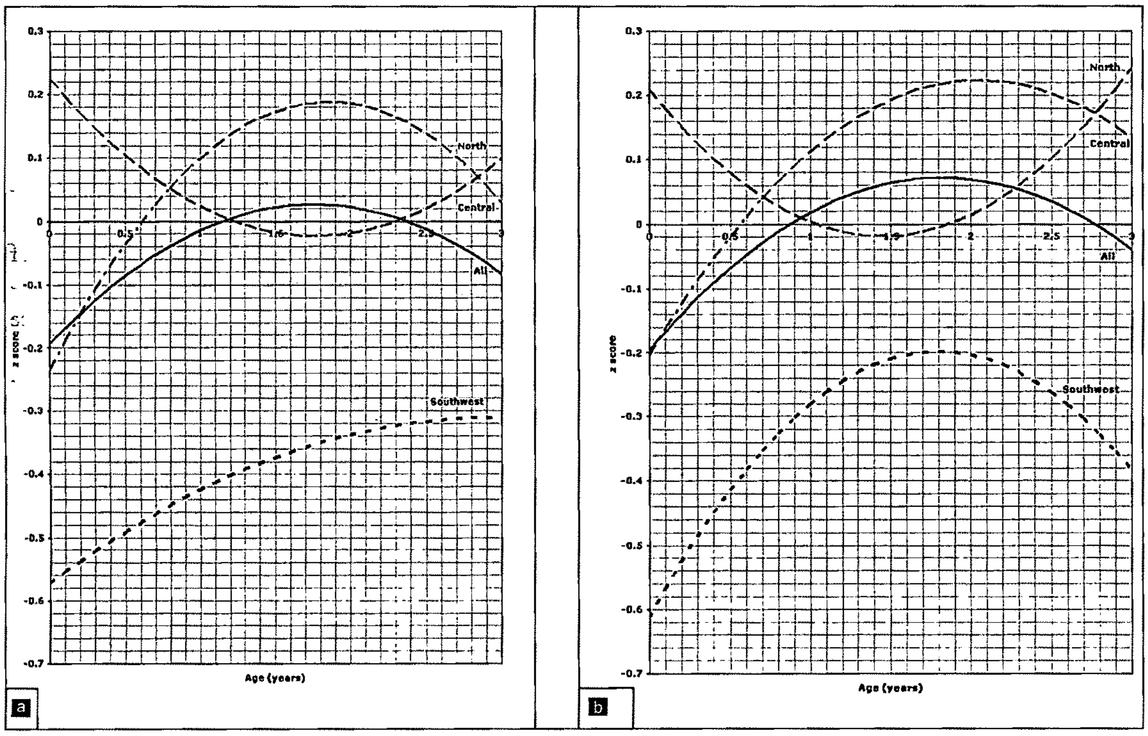

Figure 2. Length of children aged 0 to 3 years, 2a for boys, 2b for girls.

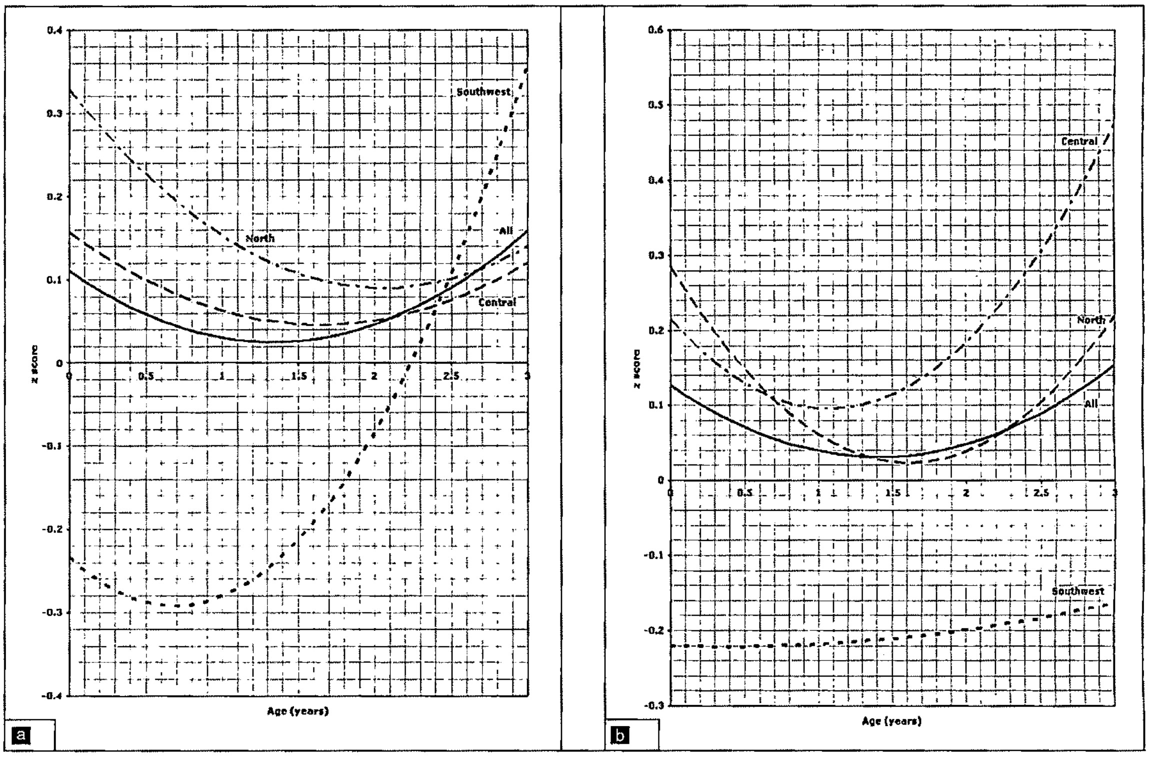

Figure 3. Head circumference of children aged 0 to 3 years, 3a for boys, 3b for girls.

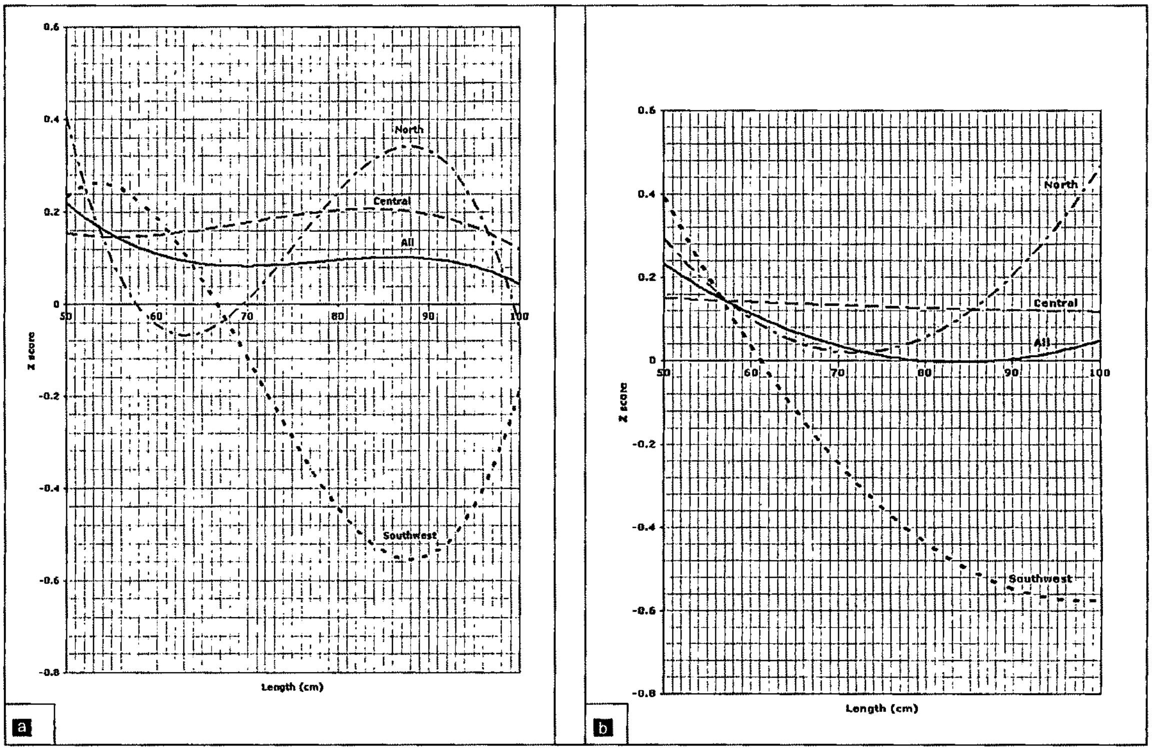

Figure 4. Weight for length of children aged 0 to 3 years, 4a for boys, 4b for girls.

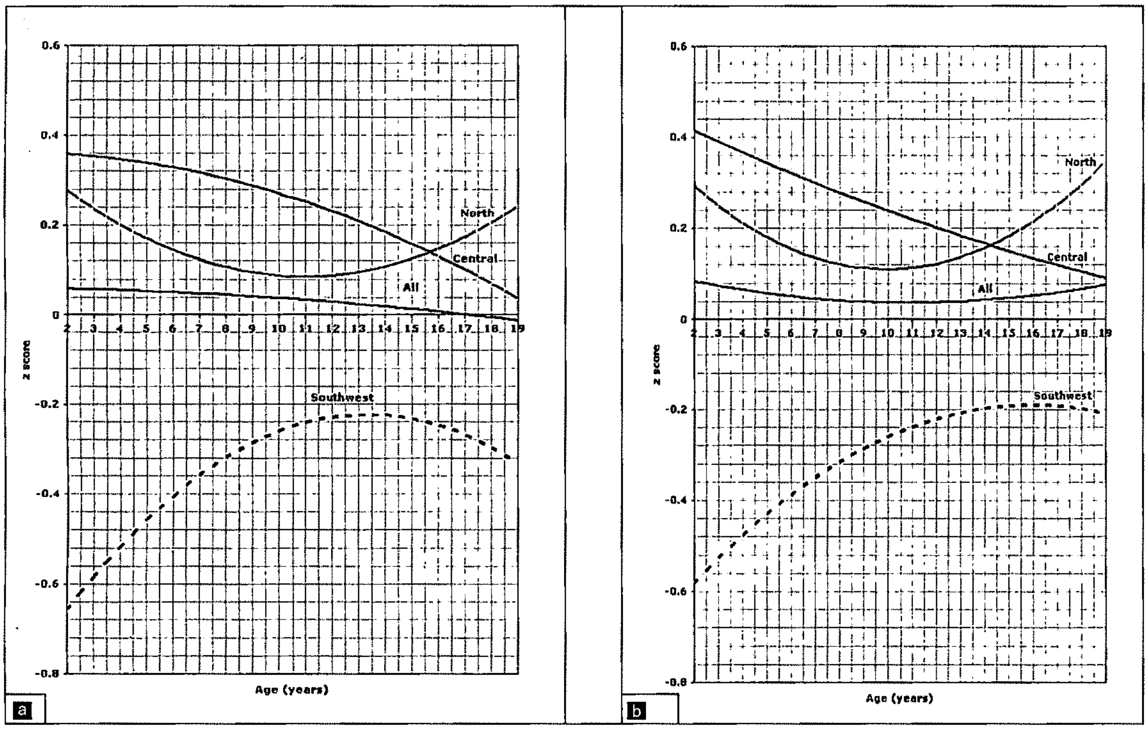

Figure 5. Weight of children aged 2 to 18 years, 5a for boys, 5b for girls.

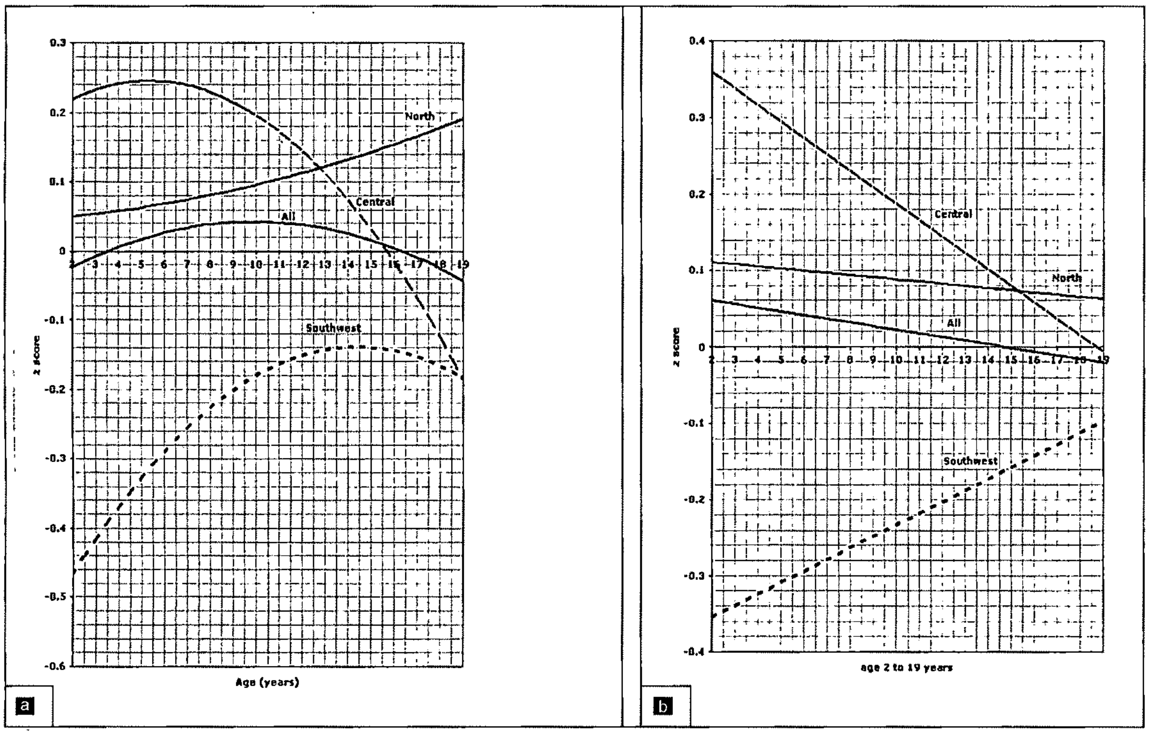

Figure 6. Stature of children aged 2 to 18 years, 6a for boys, 6b for girls.

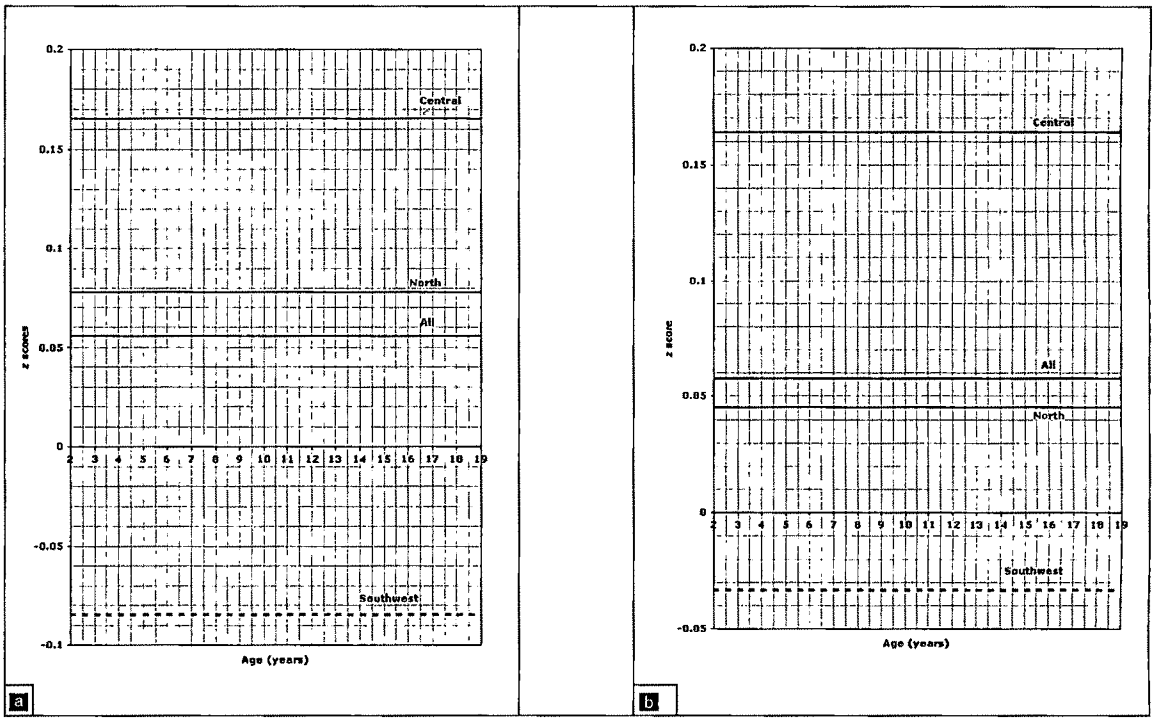

Figure 7. Head circumference of children aged 2 to 18 years, 7a for boys, 7b for girls.

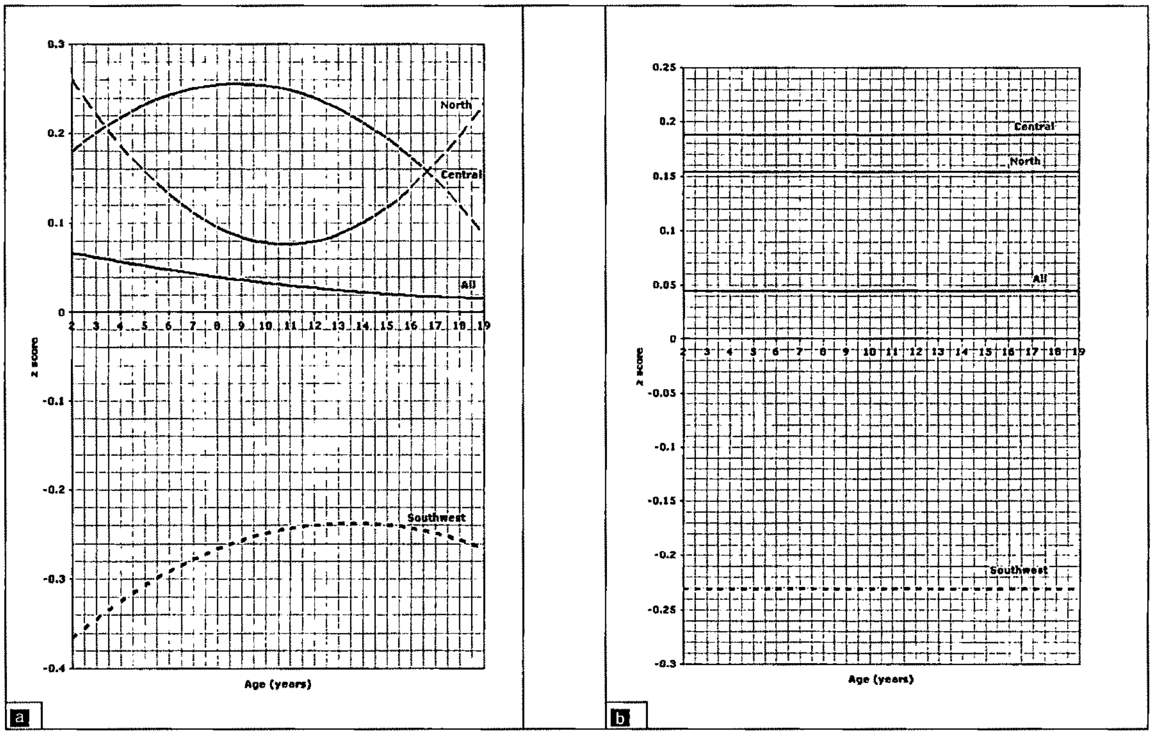

Figure 8. Body mass index of children aged 2 to 18 years, 8a for boys, 8b for girls.

DISCUSSION

It is well known that the growth of children as assessed by anthropometric measurements is affected by a combination of genetic and environmental factors. Although studies suggest a minimal role for genetic factors,[13-15] ethnic variations both between individuals and populations cannot be excluded.[16] Furthermore, variation in growth within the same country is greater than when children from different countries have the opportunity to express their full potential for growth.[17] However, this ideal situation does not exist in practice because of many factors such as disparity in socioeconomic status, availability of food, access to adequate health services, environmental hygiene, parental educational level and altitude. Regional variation in the degree of development are well known in all countries but are more important in developing countries where more resources are usually assigned to urban than more remote areas. In a study from China, comparing the effect of the reforms on the growth of children in urban and rural areas, it was concluded that despite an overall improvement in child growth during the economic reforms in China, the improvement has not been uniform, as judged by increased differences in height between rural and urban children and increased disparities within rural areas.[18]

In this report, we compare the growth of Saudi children and adolescents between three regions with different population characteristics. The central (Riyadh and Qassim), representing a majority of multiethnic population, three regions from the North (Hail, Jouf, Northern Borders), most likely to have a stable Northern tribal population. Two regions from the southwest (Aseer and Gizan) also most likely to have a majority of stable southern population that is distinct from the north.

The lower growth of children and adolescents in the southwestern population of Saudi Arabia has been assumed, but not documented or quantified. This report demonstrates significantly lower growth of children and adolescents living in southwest regions compared to those in other regions, affecting most growth parameters as indicated by consistently lower z scores. The potential causes of these variations are multiple and many of the well-known factors (environmental and genetic) affecting growth, such as the higher altitude and the predominance of rural settlements in the southwest, may be implicated. The altitude in the city of Abha for example is about 2200 meters above sea level compared to about 700 meters for the north and that of the central region.[19] In addition, rural settlements account for about 56% and 68% in Aseer and Gizan respectively, compared to about 23% in the north and central regions.[20] The size of the sample was large and representative, and weighted for the population of each region, making any effect of sample size on the observed differences between regions highly unlikely.

The implication of these differences is considerable and must be taken ino consideration in the assessment of growth of children and adolescents in the southwest who have significantly lower growth parameters than those in the central or northern regions. Further studies focusing on factors associated with lower growth of children in the southwest are needed to make recommendations for improvement in their growth.

Acknowledgment

This article is part of the Health Profile for Saudi children and adolescents supported by a grant from King Abdulaziz City for Science and Technology in Riyadh (grant No. AR-20-63).

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original article

The prevalence of metabolic syndrome and cardiovascular risk factors in a group of obese Saudi children and adolescents: a hospital-based study

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Ann Saudi Med 2009; 29(5): 357-360

BACKGROUND AND OBJECTIVES: We assessed the distribution of risk factors associated with the metabolic syndrome in a group of obese Saudi children and adolescents. No previous studies had addressed this issue in the Saudi pediatric population.

SUBJECTS AND METHODS: We retrospectively reviewed the medical records of patients evaluated for obesity between 2004 and 2008 and collected data on age, weight, height, body mass index (BMI), BP, fasting lipid profile, fasting glucose, insulin concentrations, and insulin resistance based on the homeostasis assessment model-insulin resistance (HOMA-IR) score. Obesity was defined as a BMI above the 95th percentile for age and gender and metabolic syndrome was diagnosed according to standard criteria.

RESULTS: We studied 57 obese Saudi children and adolescents with a mean (standard deviation) age of 9.8 (3.5) years. Mean weight and body mass index (BMI) were 63.7 (28.3) kg and 31.6 (8.0) kg/m^2, respectively. Systolic BP was elevated in 24 (42%) of the 57 subjects. Of the 39 children who had a lipid profile in their records, 10 had hypertriglyceridemia, 8 had hypercholesterolemia, 6 had elevated LDL cholesterol levels, and 6 had low HDL cholesterol levels. Impaired fasting glucose was found in 10 of 38 patients in which it was measured, and 9 of 25 patients had fasting hyperinsulinemia. Eleven of 37 patients (29.7%) met the diagnosis of the metabolic syndrome. Diastolic BP correlated positively with BMI ($r=0.440$, $P=.001$), and HDL cholesterol correlated negatively with weight and BMI ($r=-0.487$, $P=.002$ and $r=-0.317$, $P=.05$). HOMA-IR correlated positively with BMI and triglyceride levels and negatively with HDL cholesterol levels.

CONCLUSIONS: Obese Saudi children and adolescents have multiple risk factors associated with metabolic syndrome.

In parallel with the worldwide growing problem of obesity, there have been several reports of an increasing prevalence of childhood obesity in the Saudi population.[1,2] Obesity in childhood is associated with the development of the metabolic syndrome.[3,4] Although the endpoints for cardiovascular risk are not usually seen in childhood, the components of the insulin resistance syndrome (obesity, hypertension, dyslipidemia, and hyperinsulinemia) track from childhood into adulthood.[5] Several studies have reported a high prevalence of the metabolic syndrome risk factors in obese children and adolescents.[6,7] The prevalence of the metabolic syndrome in overweight adolescents from the United States Third National Health and Nutrition Examination Survey (NHANES III) was 28%.[6] In addition, 30% of Hispanic overweight youth with family history of type 2 diabetes had the metabolic syndrome.[7] To date, there are no published studies on the prevalence of the metabolic syndrome risk factors among Saudi children and adolescents. This study is the first to examine the extent of the metabolic syndrome in a group of obese Saudi children and adolescents.

SUBJECTS AND METHODS

Fifty-seven Saudi children and adolescents with a mean (standard deviation) age of 9.8 (3.5) years were seen in the Pediatric Endocrinology Clinic at King Faisal Specialist Hospital and Research Centre-Jeddah between 2004 and 2008 for evaluation of obesity. We systematically reviewed their medical records and extracted information on age, gender, weight, height, body mass index (BMI), blood pressure (BP), fasting glucose, fasting insulin, and fasting lipid profile. Given the retrospective nature of the study, data were missing for 20 patients for one or more of the biochemical parameters. Obesity was defined as a BMI above the 95th percentile for age and gender.[8] Exclusion criteria included obesity associated with genetic syndromes, the presence of diabetes, diseases and/or medications that alter BP or lipid metabolism. Hypertension was defined as a systolic BP and/or diastolic BP>95th percentile by gender, age, and height.[9] Abnormalities in fasting levels of triglycerides, cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol were adjusted for age and sex (>95th percentile for triglycerides, cholesterol, LDL; and <5th percentile for HDL).[10] The reference value for elevated fasting plasma glucose (FPG) was taken from the American Diabetes Association guideline of >5.6 mmol/L.[11] The diagnosis of the metabolic syndrome was defined according to the Third Report of the National Cholesterol Education Expert Panel-Adult treatment Panel (NCEP-ATP III) criteria[12] and the World Health Organization criteria,[13] modified for children. The subjects were classified as having the metabolic syndrome if they met three or more of the following criteria for age and sex: BMI>95th percentile, triglyceride level >95th percentile, HDL cholesterol level <5th percentile, systolic or diastolic BP>95th percentile, and impaired fasting glucose. The degree of insulin resistance was estimated (fasting glucose [mmol/L]× fasting insulin [μU/mL]÷22.5) using the homeostasis assessment model- insulin resistance (HOMA-IR) score with higher scores indicating greater insulin resistance.[14]

Table 1. Anthropometric and metabolic characteristics of subjects (n=57).

Characteristic	Mean (SD)	Number (%) of children with abnormalities
Age (years)	9.8 (3.5)	N/A
Weight (kg)	63.7 (28.3)	57/57 (100%)
BMI (kg/m^2)	31.6 (8)	57/57 (100%)
BMI z score	3.5 (0.7)	57 /57(100%)
Systolic BP (mm Hg)	118.6 (13.2)	24/57 (44%)
Diastolic BP (mm Hg)	67.3 (7.4)	2/57 (3.5%)
Triglycerides (mmol/L)	1.0 (0.5)	10/39 (25.6%)
Total cholesterol (mmol/L)	4.3 (0.9)	8/39 (20.5%)
LDL cholesterol (mmol/L)	2.8 (0.7)	6/39 (15.4%)
HDL cholesterol (mmol/L)	1.3 (0.4)	6/39 (15.4%)
Fasting glucose (mmol/L)	5.2 (0.5)	10/38 (26.3%)
Fasting insulin (pmol/L)	147.6 (101.8)	9/25 (36%)

N/A= not applicable

Data is presented as means (standard deviation). Pearson's correlation analysis was used to study the relationship between variables. Statistical significance was considered at $P<.05$.

RESULTS

The mean age of the subjects was 9.8 (3.5) years; 33 (57.9%) were males. Mean weight and BMI were 63.7 (28.3) kg and 31.6 (8.0) kg/m^2, respectively. All subjects had a BMI above the 95th percentile for age and sex. The BMI Z score averaged 3.5 (0.7). Table 1 shows the anthropometric and metabolic characteristics of the subjects. Twenty-four of the 57 children (44%) had a systolic BP above the 95th percentile for age and height, and only two children had a diastolic BP above the 95th percentile for age and height. Of the 39 children who had a lipid profile in their records, 10 (25.6%) had hypertriglyceridemia, 8 (20.5%) had hypercholesterolemia 6 (15.4%) had elevated LDL cholesterol levels, and 6 (15.4%) had low HDL cholesterol levels for age and sex. Impaired fasting glucose was found in 10 of 38 patients (26.3%), and 9 of 25 patients (36%) tested had hyperinsulinemia. Males and females did not differ significantly in any of the anthropometric or biochemical parameters.

Among the 37 subjects who had all data available, 15 (40%) had two components of the metabolic syndrome, 6 (16%) had three components, 4 (11%) had four components, and one had all of the five components. Eleven of the 37 subjects (29.7%) met the diagnosis of metabolic syndrome. In addition, 9 of the 20 subjects (45%) with missing biochemical data had two components of the metabolic syndrome.Weight and BMI correlated positively with age (r=0.756, $P<.001$ and r=0.528, $P<.001$ respectively). Also, diastolic BP correlated positively with BMI (r=0.440, $P=.001$). HOMA-IR correlated positively with weight (r=0.513, $P=.01$), BMI (r=0.619, $P=.001$), and triglyceride levels (r=0.461, $P=.03$); and correlated negatively with HDL cholesterol levels (r=−0.481, $P=.03$). HDL cholesterol correlated negatively with weight and BMI ($r=-0.487$, $P=.002$ and $r=-0.317$, $P=.05$).

DISCUSSION

The metabolic syndrome is defined as a cluster of cardiovascular disease risk factors that include abdominal obesity, diabetes and raised fasting glucose concentrations, dyslipidemia, and hypertension.[12,13] Although a uniform definition of the syndrome in pediatrics is lacking, several studies have shown that the syndrome develops in childhood and is prevalent among overweight children and adolescents.[6,7]

The prevalence of obesity in Saudi children has been increasing over the past few decades. A recent study of trends in the nutritional status of Saudi children comparing growth data collected between 1993 and1994 with those collected between 2004 and 2005 from all regions of Saudi Arabia reported a tendency toward overweight and obesity over the last decade.[15] Another study reported an increase in the proportion of obese schoolboys from 3.4% in 1988 to 24.5% in 2005.[16]

Our study is the first to demonstrate a high prevalence of the metabolic syndrome and its components in a group of obese Saudi children. Thirty percent of obese Saudi children in our study had three or more of the components of the metabolic syndrome and therefore met the criteria for the diagnosis of the metabolic syndrome. The overall prevalence of the metabolic syndrome in adolescents in the United States was 4.2% while the prevalence in obese adolescents was 28.7%.[6] In addition, 89% of overweight US adolescents had at least one abnormality of the metabolic syndrome and 56% had two components of the metabolic syndrome.[6] Our data correlate with international data[6,7] and suggest that a substantial number of Saudi children may have the metabolic syndrome. Insulin resistance correlated with the degree of obesity; this emphasizes the central role that obesity plays in the development of insulin resistance. Furthermore, the correlation of insulin resistance with the various components of the metabolic syndrome in our study highlights the importance of insulin resistance in the pathophysiology of the syndrome in childhood.

Hyperinsulinemia, dyslipidemia, hypertension, and impaired fasting glucose seem to be highly prevalent in obese Saudi children. Epidemiological evidence suggests that the clustering of the metabolic syndrome components extends strongly into adult life.[17] Also, the pathological processes associated with the development of atherosclerotic cardiovascular disease, fatty streaks and fibrous plaques in the aorta and coronary arteries, have been shown to begin during childhood.[18] With these cardiovascular risk factors manifesting in childhood, earlier presentation of cardiovascular events will emerge as a major and challenging public health problem. Pediatricians need to be alerted regarding the existence of the metabolic syndrome in obese children. In addition, screening for the various components of the syndrome in obese children and early intervention are recommended. Further research is needed to determine the effectiveness of prevention and of various lifestyle and pharmacologic interventions in the management of the metabolic syndrome in children.

Our results have to be interpreted in the context of the limitations of a hospital-based retrospective analysis with some missing data in addition to a small sample size. A large population based study is recommended to establish the prevalence of the metabolic syndrome and its components in Saudi obese and nonobese children.

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original article

Pediatric retinal detachment in the Eastern Province of Saudi Arabia: experience of a tertiary care hospital

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Ann Saudi Med 2009; 29(5): 361-364

BACKGROUND AND OBJECTIVES: Because no previous studies have addressed the issue, we describe clinical characteristics and surgical outcome of patients with rhegmatogenous retinal detachment (RRD) in a pediatric population of the Eastern province of Saudi Arabia.

PATIENTS AND METHODS: We conducted a retrospective review of all consecutive cases of pediatric RRD (0-18 years) patients presenting at Dhahran Eye Specialist Hospital, a tertiary care hospital, in the Eastern Province of Saudi Arabia over a period of 3 years.

RESULTS: Twenty patients were included in the study, accounting for 9.4% of all retinal detachment surgery cases performed over a period of 3 years (January 2006 to December 2008). The median age was 11.0 years, (range, birth to 18 years). Trauma, (45%) myopia/vitreoretinal degeneration (10%) and prior ocular surgery (25%) were significant risk factors for RRD. Proliferative vitreoretinopathy (PVR) more than grade C was present in 14/20 (70%) of cases. Most patients (15/20, 75%) were treated with pars plana vitrectomy and placement of an encircling buckle, while silicone oil or gas was used as tamponade in 13/20 (65%) patients. Surgery was successful in 17/20 (85%) cases in achieving retinal re-attachment. Visual acuity improved significantly following surgery (Mean preop 2.146 LogMAR, Mean postop 1.497 LogMAR) (P=.014). Longer duration of RRD (P=.007) and macular involvement (P=.05) were associated with worse anatomical outcomes following surgery.

CONCLUSION: Pediatric RRD in the Eastern province is often associated with predisposing pathology. Surgery is successful in achieving anatomical reattachment of the retina in a majority of cases with improvement of visual acuity.

Pediatric rhegmatogenous retinal detachment (RRD) accounts for 2.0% to 6.6% of all RRD cases.[1-3] In contrast to RRD in adults, children usually present late and have clinical features attributable to a longstanding retinal detachment such as macular involvement and proliferative vitreoretinopathy (PVR).[4] Consequently, guidelines obtained from studies of adult cases may be inappropriate for applying to management of pediatric RRD. No previous studies describing clinical features and surgical outcome of pediatric patients with RRD have been reported in Arabian patients. We report clinical features and surgical outcome of pediatric RRD on a consecutive series of patients undergoing retinal redetachment surgery in the eastern province of Saudi Arabia.

PATIENTS AND METHODS

We conducted a retrospective chart review of all consecutive pediatric patients (younger than 18 years of age) who had surgery for retinal detachment at the Dhahran Eye Specialist Hospital, a tertiary care hospital in the eastern province of Saudi Arabia, during a period of 36 months from January 2006 to December 2008. Patients in the study were identified by an operating room log, and all operations were performed by a single experienced vitreoretinal surgeon (RAC).

A total of 20 patients were included in the study.

Table 1. Preoperative characteristics.

Number of patients	20
Age	Mean=8.68 years; SD=7.007; Median=11.0 years
	(Range: 0.1-18.0)
Sex	
Male	14 (70%)
Female	6 (30%)
Preoperative visual acuity	Mean=2.146 LogMAR
	(Range=0-3.0)
Lens status	
Phakic	15 (75%)
Aphakic	4 (20%)
Pseudophakic	1 (5%)

Table 2. Clinical characteristics of retinal detachment.

Number of retinal breaks	
>2 tears	8 (40%)
Not seen	6 (30%)
One tear	6 (30%)
Type of retinal breaks	
Retinal tear	13 (65%)
Retinal hole	3 (15%)
Giant retinal tear	3 (15%)
Retinal dialysis	1 (5%)
PVR (>Grade C)	
Present	14 (70%)
None	6 (30%)

Clinical records of patients were reviewed and information regarding age, sex, preoperative visual acuity (Snellen converted to LogMAR), characteristics of retinal detachment, retinal tears, surgical procedures, tamponade, lens status, predisposing ocular conditions, PVR and prior intraocular surgery, final visual acuity and retinal reattachment status of last patient visit was recorded. Four patients with less than three months of postoperative follow-up were excluded from the study.

Statistical analysis of results was done with SPSS statistical software (version 13.0.1, Professional Statistics Release, Chicago, USA). The Wilcoxen signed ranks test was used for comparison of means for numerical data and the Fisher exact test for categorical data. A significance level of .05 was used in this study.

RESULTS

A total of 20 patients were included in the study (14 males, 6 females), and they accounted for 9.4% of all retinal detachment surgery cases performed over a period of 3 years. The duration of postoperative follow-up ranged from 6 to 36 months (mean, 24.4 months). Table 1 shows the demographics of the patients. Table 2 shows clinical features of retinal detachment at presentation. The retinal detachment was total or subtotal at presentation in most patients (17/20), with macular involvement in over half of the patients. The duration of retinal detachment was unknown in 12/20 (60%) of patients, while 4/10 (20%) patients had retinal detachment for less than two months duration and 4/20 (20%) had retinal detachement for than two months. PVR more than grade C was present in 14/20 (70%) of cases. The main predisposing factors associated with retinal detachment included blunt trauma (9/20, 45%), prior intraocular surgery (5/20, 25%) and myopia/vitreoretinal degeneration (4/20, 20%). Two cases (2/20, 10%) were not associated with any identifiable predisposing condition, while retinopathy of prematurity (1/20, 5%) and Stickler syndrome (1/20, 5%) were responsible for others. Table 3 shows type of surgical procedure performed. Most patients (15/20, 75%) were treated with internal approach with pars plana vitrectomy in association with placement of encircling buckle, while silicone oil or gas used as tamonade in 13/20 (65%) patients. Successful retinal reattachment was obtained in 17/20 (85%) cases, which was reflected in improvement of mean visual acuity (P=.018) from preoperative levels.

Table 4 shows factors associated with worse anatomical outcome. Two factors were associated with worse anatomical outcomes. These included macular detachment (P=.05) and longer duration of retinal detachment (P=.007) at presentation. Although not statistically significant, a trend of worse anatomical outcome was also seen in patients in whom retinal breaks were not seen or more than two retinal breaks were present. (P=.089)

DISCUSSION

Pediatric RRD is much less common than adult retinal detachment. In our institution, a tertiary care ophthalmology facility that serves a catchment population of approximately 5 million, accounted for 9.4% of all retinal detachment surgery cases performed over a period of 3 years. This incidence is higher than reported in studies from other parts of the world. Yokoyama et al[5] found an incidence of 3.1% of pediatric RRD (age 0-15 years; mean 12 years) of all RRD cases in the Japanese population, while Rumelt et al[6] found an incidence of 6.6% (age 0-18 years; mean 10.8 years) in a mixed Middle Eastern population of mainly Caucasian descent. This higher incidence in our study may be related to factors such as a higher incidence of inherited myopia/vitreoretinal degeneration in children and ocular trauma in pediatric population due to socioeconomic factors in Saudi Arabia.

Like studies reported from other parts of the world, most pediatric patients in our study were male (14/20, 70%). Blunt trauma was the most notable cause of retinal detachment, responsible for 9/20 (45%) cases. This is higher than reported in other studies[6] and may be due to a higher incidence of ocular trauma in Saudi Arabia.[8] Myopia and vitreoretinal degeneration are more common in the Arabian population due to hereditary factors, and this was reflected in our study with 4/20 (20%) cases[9,10] of retinal detachment associated with myopia.

The type of surgical procedure for management of pediatric retinal detachment depends on choice of surgeon and is also dictated by the presence or absence of PVR. We opted to treat most patients with a combination of pars plana vitrectomy and encircling explant, as PVR was present in most patients (14/20, 70%). Since most patients (16/20, 80%) had retinal detachment of more than two months duration and PVR, a combination of PPV and encircling buckle, allowed optimal relief of vitreoretinal traction for successful retinal re-

Table 3. Surgical procedure.

Type of surgical procedure	
PPV+SB	15 (75%)
Scleral buckle (SB)	4 (20%)
Pars plana vitrectomy (PPV)	1 (5%)
Tamponade used	
Silicone oil	9 (45%)
None	7 (35%)
Gas. (C3F8)	4 (20%)

Table 4. Factors associated with worse anatomical outcome.

Risk factors	Retina attached		*P* value
	Yes	No	
All patients	17	3	
Preoperative characteristics			
Age (Mean years, range)	9.25 (0.2-18)	5.43 (0.1-16)	.380
Sex			
Male	12	2	.681
Female	5	1	
Lens status			
Phakic	13	2	.601
Aphakic	3	1	
Pseudophakic	1	0	
Characteristics of RRD			
Macula status at diagnosis			
On	10	0	.050
Off	7	3	
Duration			
>3 months	12	0	.007
>2 months	1	3	
<2 months	4	0	
Extent of RD			
Total	5	3	.155
Subtotal	9	0	
Inferior	2	0	
Superior	1	0	
Number of breaks			
Not seen	6	0	.089
>2	6	3	
One	5	0	
Type of retinal break			
Tear	11	2	.749
Hole	3	0	
Dialyses	1	0	
Giant tear	2	1	
PVR			
None	6	0	.521
Present	11	3	

attachment. Statistical analysis of factors associated with anatomical outcome (Table 4) following surgery showed that macular detachment (P=.05) and longer duration of retinal detachment (P=.007) were associated with worse anatomical outcome. A trend of worse anatomical outcome, though not statistically significant (P=.089), was also seen when retinal breaks were not seen or more than two retinal breaks were present. These findings are consistent with other studies[4,11] in that early surgical treatment of retinal detachment is more likely to be successful before significant PVR sets in.

The anatomical and functional results of this study are encouraging. We achieved retinal reattachment in 17/20 (85%) cases, and visual acuity showed significant improvement from preoperative levels (P=.018). This is comparable with results reported from other studies. Our study is limited by small numbers and retrospective nature of data collection. However, the results of this study are important for documenting clinical features and management plans in Saudi population, where no previous data exists for such a condition.

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original article

Prevalence of oral lesions among Saudi dental patients

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Accepted for publication August 2008

Ann Saudi Med 2009; 29(5): 365-368

BACKGROUND AND OBJECTIVES: Few studies have been conducted in the Saudi population on oral mucosal lesions. The purpose of this study was to evaluate the type and extent of oral lesions in a study among dental patients at a college of dentistry in Saudi Arabia.

PATIENTS AND METHODS: Over a 3-year period, 2552 dental outpatients were interviewed and investigated clinically for the presence of oral mucosal conditions. A thorough oral clinical examination was performed, including a radiographic examination. The diagnosis was confirmed histopathologically when necessary.

RESULTS: Of 383 (15.0%) patients found to have oral mucosal lesions, females constituted 57.7% (n=221) and males 42.3% (n=162). The age range of the patients was between 15 to 73 years with a mean age of 38.2 years. The most commonly affected age group was 31 to 40 years, which comprised 21.4% (n=82) of all affected individuals. The least affected age group were individuals older than 61 years. The most common lesion was Fordyce granules (3.8%; n=98), followed by leukoedema (3.4%; n=86) and traumatic lesions (ulcer, erosion) in 1.9% (n=48). Tongue abnormalities were present in 4.0% (n=101) of all oral conditions observed, ranging from 1.4% (n=36) for fissured tongue to 0.1% (n=2) for bifid tongue. Other findings detected were torous platinus (1.3%; n=34), mandibular tori (0.1%; n=2) aphthous ulcer (0.4%; n=10), herpes simplex (0.3%; n=7), frictional hyperkeratosis (0.9%; n=23), melanosis (0.6%; n=14), lichen planus (0.3%; n=9) and nicotinic stomatitis (0.5%; n=13).

CONCLUSION: The findings of this study provide information on the types and prevalence of oral lesions among Saudi dental patients. This provides baseline data for future studies about the prevalence of oral lesions in the general population.

Few studies have been conducted in the Saudi population on oral mucosal lesions. An 8-year retrospective study using biopsied specimens found that focal fibrous hyperplasia (FFH), pyogenic granuloma (PG), peripheral giant cell granuloma (PGCG) and peripheral ossifying fibroma (POF) constitute 9% of all biopsied lesions.[1] A 5-year (1985-1990) survey in Saudi Arabia indicated that 64.6% of biopsied lesions were benign tumors, hyperplasia and granulomas, 20.3% were cysts and cyst-like lesions and 4.8% were other mucous membrane lesions.[2]

The prevalence of leukoplakia was studied in relationship to tobacco habits and was found to be 11.4% in the Gizan area of Saudi Arabia.[3,4] The oral cavity was ranked as one of the most common ten malignancies from 1975-2006.[5] The tongue was the most affected site (30.1%), mostly on the lateral borders of the anterior two-thirds, followed by the oropharynx, lips, cheeks, gingiva and floor of the mouth, palate and salivary gland.[6] Oral health survey data are essential for proper health planning programs. In addition, most of the conducted studies were of tumors or ulcers and did not include all oral lesions in adult populations. The pattern of disease is also changing due to increasing awareness, changes in lifestyle and increasing interest in oral health. In Saudi Arabia there is a great need for clinical studies to establish baseline data on the prevalence of oral lesions. The aim of this study was to determine the type and the prevalence of oral lesions among patients seeking dental care.

PATIENTS AND METHODS

This study was carried out on adult Saudi dental outpatients who attended the Oral Diagnostic Clinic at the College of Dentistry, King Saud University, Riyadh, Saudi Arabia, for an oral examination and a dental treatment plan. The study sample included adult subjects who were older than 15 years of age. The college is an open public facility and referral hospital. A total of 2552 patients were interviewed and clinically investigated for the presence of oral lesions from June 2002- to December 2005. History taking and a thorough oral clinical examination was performed, including a radiographic examination. The type and distribution of the oral mucosal conditions was recorded. An interview was conducted to collect information. The examination was performed by a single examiner. Data were statistically analyzed using SPSS (SPSS, Inc. Chicago, IL).

RESULTS

Among the 2552 patients, only 383 patients (15.0%) had oral lesions. Females constituted 57.7% (n=221) and males 42.3% (n=162). The age range of the patients was between 15 to 73 years. The mean age of the sample group was 38.2 years. The mean age for females was 33.0 years and 47.1 years for males. Of the total sample, the most commonly affected age was between 31 to 40 years (21.4%), followed by 15 to 20 years (18.5%), and 21 to 30 years (17.8%) (Figure 1). Twenty-four patients (0.9%) admitted smoking habits and 196 patients (7.7%) had a systemic disease, but there were no differences between smokers and non-smokers, or between healthy people and those with systemic diseases.

Oral lesions were more prevalent among females than males (Table 1). Fordyce granules were observed in 3.84% (n=98) on the buccal and labial mucosa, and were significantly more common in females. Females showed a higher prevalence than males, accounting for two-thirds of the affected individuals (n=24), but the difference was not statistically significant. Both torous platinus and mandibular tori wre more common in females, but the difference was not statistically significant. Other lesions were significantly more common among females: aphthous ulcer and herpes simplex. On the other hand, frictional hyperkeratosis was more common among males than females, but the difference was not statistically significant. Other pathologies detected were excessive melanin pigmentation (melanosis). Females showed a higher incidence than males, but the difference was not statistically significant. Both lichen planis and nicotinic stomatitis were significantly higher among males.

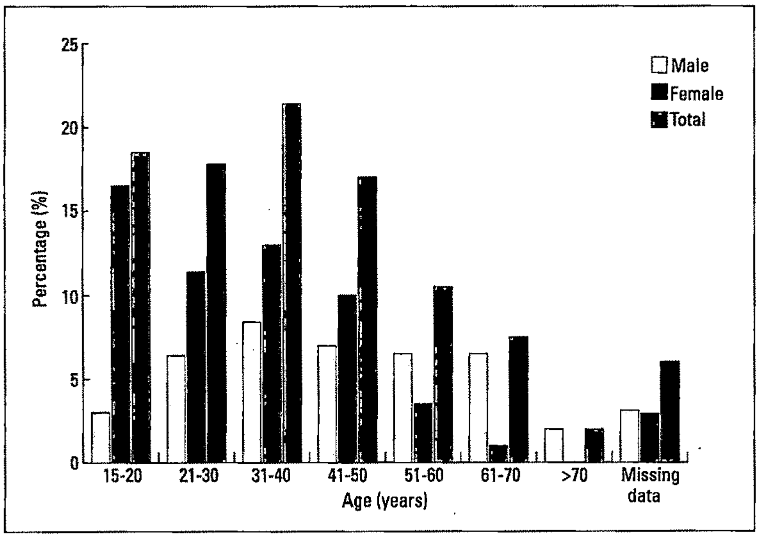

Figure 1. Prevalence of oral conditions by age range and sex (n=383).

Tongue abnormalities were present in 3.96% (n=101) of total sample and in 26.4% of all oral conditions observed. The prevalence of tongue lesions was higher among females than males, but the difference was not statistically significant. the most common tongue condition was fissured tongue, constituting about 35.6% of all tongue conditions. it is also ranked fourth most common lesion in our population. Hairy tongue was present in 0.55% of the sample (n=14) and was significantly more common in males than in females. Tongue tie was also significanlty more common in females than males. Other tongue lesions were lingual varcosis. Females showed a higher incidence than males, but the difference was no statistically significant. Both bifid tonge and glossitis had a low occurrence and were seen manily among females.

DISCUSSION

Oral soft tissue lesions present a significant health problem with a considerable morbidity. Despite its importance, there are few reports on its prevalence among the Saudi population and its association with oral habits, when compared to dental caries and periodontal diseases.

In accordance with others,[1,2] our results showed a higher prevalence of oral mucosal lesions among females (57.7%) and young adults (31-40 years) (21.4%). Other reports, however, indicated that oral lesions tend to increase with age in association with tobacco consumption and denture use.[7,8] The age of the patient is crucial in patient assessment, treatment planning and health education.

The present study suggests the distribution pattern of oral diseases in Saudi Arabia is similar to other countries. Benign lesions are more common in the young and females while cancerous and precancerous lesions are more common in the elderly.[9,10] Along with other investigations,[1-6,11] it may also shed some light on the pattern

Table 1. Distribution of oral conditions in Saudi dental patients (n=2552).

Type	Males		Females		Total	
	No.	% of total sample	No.	% of total sample	No.	% of total sample
Fordyce granules[a]	30	1.18	68	2.67	98	3.84
Leukoedema[b]	53	2.08	33	1.29	86	3.37
Traumatic lesions (ulcers, erosions)	14	0.55	34	1.33*	48	1.88
Torous platinus	0	0	34	1.33	34	1.33
Frictional hyperkeratosis	14	0.55	9	0.35	23	0.90
Melanosis	5	0.195	9	0.35	14	0.55
Nicotinic stomatitis[a]	11	0.43	2	0.08	13	0.51
Aphthae[a]	0	0	10	0.39	10	0.39
Lichen planus	7	0.27	2	0.08	9	0.35
Herpes simplex[c]	0	0	7	0.27	7	0.27
Mandibular tori	0	0	2	0.08	2	0.08
Non-nicotinic stomatitis	2	0.08	2	0.08	4	0.16
Focal fibrous hyperplasia	2	0.08	3	0.12	5	0.195
Tongue lesions						
Fissured tongue	12	0.47	24	0.94	36	1.41
Bifid tongue	0	0	2	0.08	2	0.08
Glossitis	0	0	3	0.12	3	0.12
Scalloped tongue	0	0	8	0.31	8	0.31
Lingual varcosis	2	0.08	8	0.31	10	0.39
Geographic tongue	7	0.27	6	0.24	13	0.51
Hairy tongue[c]	10	0.39	4	0.16	14	0.55
Tongue tie	2	0.08	12	0.47	15*	0.59
Total tongue lesions	33	1.3	67	2.6	101	3.96
Total	171		282		454	

*One case missing sex; [a]$P<.005$, [b]$P=.0001$, [c]$P<.05$ males vs. females

of oral diseases among the Saudi population. Reports from different regions of Saudi Arabia have shown that cancer and precancerous lesions are more common in elderly males[3-6,11] in contrast to benign lesions, which are more common in females at a younger age.[1,2]

As in the report of Kovac-Kovacic and Skaleric in Slovenia,[10] Fordyce granules were the most common oral condition and had a female predilection (10%). This lesion was not as common among Amazonian Indians (3.8%).[12] Leukoedema was found to have a high prevalence among our study population. Similar findings have been reported among Kenyans (26%), the Swedish population (49.07%) and in the institutionalized elderly in South Africa (24.4%).[13-15] In contrast, leukoedema was not reported as one of the common soft tissue conditions among elderly Chinese.[16] As in other studies, males were significantly more affected than females.[11,17] Studies have demonstrated a positive association between smoking, tobacco use and leukoedema with a decline the size of the lesion after tobacco cessation.[17-20] Though not clear in our results, this may in general explain the male predominance of this condition.

Traumatic ulcer was the third most common soft tissue lesion. Females were affected more than males. It was also found to be one of the common soft tissue lesions in Spain, Italy, and Chile elderly and in the institutionalized elderly in Denmark.[21-24] The main reason among the elderly was poorly constructed dentures.[23-25]

As in the to Kenya[13] and in elderly Malaysians,[26] frictional hyperkeratosis ranked as one of the most common oral mucosal lesions. This finding supports the results from the United States of America,[27] China[28] and Bangladesh,[29] where keratotic lesions are a common clinical presentation possibly due to population differences, particularly in term of tobacco habits.

Consistent with data from China,[28] tongue conditions were a frequent observation in our study, comprising almost one-third of the mucosal lesions. Fissured tongue ranked fourth among oral abnormalities and was the most common tongue conditions. Worldwide, fissured tongue occurrence varies, but remains a common tongue condition ranging from 28% among elderly Thai,[30] 27.3% among Amazonians,[12] 21.1% among Slovenians[10] and 5.2% in Turkey.[31] Fissured tongue was also one of the common tongue conditions, constituting 45.7% in Jordan.[32]

The findings of this study possibly provide important and missing information about the types and prevalence of oral lesions among Saudi dental patients and can serve as baseline data for future studies on the prevalence of different oral lesions in the general population.

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Management of ascites due to gastrointestinal malignancy

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Accepted for publication March 2009

Ann Saudi Med 2009; 29(5): 369-377

Ascites is the pathological accumulation of fluid within the abdominal cavity. The most common cancers associated with ascites are adenocarcinomas of the ovary, breast, colon, stomach and pancreas. Symptoms include abdominal distension, nausea, vomiting, early satiety, dyspnea, lower extremity edema, weight gain and reduced mobility. There are many potential causes of ascites in cancer patients, including peritoneal carcinomatosis, malignant obstruction of draining lymphatics, portal vein thrombosis, elevated portal venous pressure from cirrhosis, congestive heart failure, constrictive pericarditis, nephrotic syndrome and peritoneal infections. Depending on the clinical presentation and expected survival, a diagnostic evaluation is usually indicated as it will impact both prognosis and the treatment approach. Key tests include serum albumin and protein and a simultaneous diagnostic paracentesis, checking ascitic fluid, WBCs, albumin, protein and cytology. Median survival after diagnosis of malignant ascites is in the range of 1 to 4 months; survival is apt to be longer for ovarian and breast cancers if systemic anti-cancer treatments are available.

The word ascites is of Greek origin (askos) and means bag or sac. Ascites is defined as the pathological accumulation of excessive fluid within the peritoneal cavity.[1] Ascitic fluid can put pressure on the diaphragm and cause difficulty in breathing. Healthy men have little or no intraperitoneal fluid, but women may normally have as much as 20 mL depending on the phase of the menstrual cycle. Malignant ascites, the subject of this review, is a manifestation of end-stage events in a variety of cancers and is associated with significant morbidity. Malignant ascites accounts for about 10% of all cases of ascites and is usually caused by ovarian, endometrial, breast, esophageal, gastric, colorectal, lung, pancreatic, hepatobilliary and primary peritoneal carcinomas.[2-4] Sometimes ascites is the sole manifestation of internal malignancies.

Pathophysiology

The most common causes of ascites are related to portal hypertension, which is usually related to liver cirrhosis. Although lymphatic obstruction is considered the major pathophysiologic mechanism behind the formation of ascites, recent evidence suggests that immunomodulators, vascular permeability factors and metalloproteinase contribute significantly to the process (Figure 1).[1] The most acceptable theory for ascites formation is peripheral arterial vasodilatation leading to underfilling of circulatory volume.

Clinical manifestations

The usual clinical presentation is a protuberant abdomen with discomfort, difficulty in breathing, fever and pain. Sometimes the hidden GI malignancy presents with ascites only. It is known that about 50% of patients with malignant ascites present with ascites at the initial diagnosis of their cancer.[5,6] The onset and progression of malignant ascites is associated with deterioration in quality of life (QoL) and a poor prognosis. According to the International Ascites Club, severity is classified as grade 1, 2 or 3 (Table 1).[7-9] Based on associated complications like spontaneous bacterial pneumonitis (SBP) or hepatorenal syndrome (HRS) and therapeutic response, it can also be classified, as uncomplicated, complicated and refractory ascites.

Diagnosis

Lab findings

Routine blood work may be inconclusive, while some tests suggest specific etiologies. A prothrombin time (PT), activated partial thrombin time (APTT) and international normalized ratio (INR) must be done prior to paracentesis in all patients. Although serum tumors markers have low diagnostic specificity, they can be used for early detection. CEA antigen is used to detect relapses of colorectal cancer, but is also expressed in pancreatic, lung and breast cancers.[9] Similarly, levels of cancer antigen 125 may be elevated in ovarian, pancreatic, lung or breast cancer.[9] Ascitic fluid analysis is essential for the diagnosis of malignant ascites (Table 2).

Fluid analysis

Ascitic fluid analysis is essential for the diagnosis of malignant ascites. Exudative or transudative ascities on the basis of total protein content (≥2.5 or <2.5 g/dL, respectively,[10] is hampered by a large overlap between malignant and non-malignant ascites. Up to 25% of patients with cirrhosis (mostly those with cardiac cirrhosis) can have high protein levels in ascites, and 18% of malignant ascites can be low in protein levels by nature.[11]

The serum-to-ascites albumin gradient (SAAG) accurately identifies the presence of portal hypertension and is more useful than the protein-based exudate/transudate concept.[12] The SAAG is easily calculated by subtracting the ascitic fluid albumin value from the serum albumin value, which is obtained on the same day. The presence of a gradient of >1.1 g/dL (>11 g/L) indicates that the patient has portal hypertension with 97 percent accuracy.[12] A gradient <1.1 g/dL (<11 g/L) indicates that the patient does not have portal hypertension.[12] The SAAG need not be repeated after the initial measurement (Table 3).

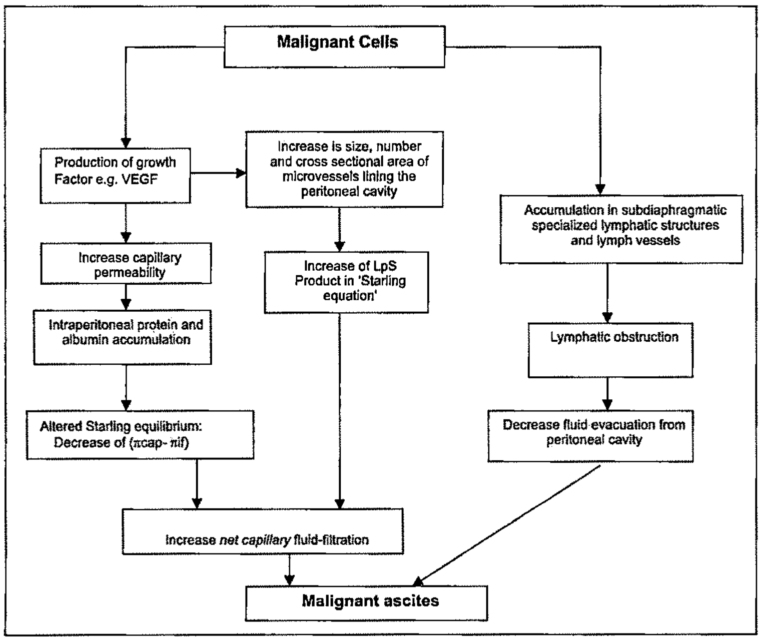
Malignant Cells
Production of growth Factor e.g. VEGF
Increase is size, number and cross sectional area of microvessels lining the peritoneal cavity
Accumulation in subdiaphragmatic specialized lymphatic structures and lymph vessels
Increase capillary permeability
Increase of LpS Product in 'Starling equation'
Intraperitoneal protein and albumin accumulation
Lymphatic obstruction
Altered Starling equilibrium: Decrease of (πcap- πif)
Decrease fluid evacuation from peritoneal cavity
Increase net capillary fluid-filtration
Malignant ascites

Figure 1. Pathophysiology of ascites.

Excellent discrimination between ascites due to liver disease or malignancy is reportedly provided by ascitic fluid fibronectin (sensitivity, 100%; specificity, 100%) and cholesterol levels,[12,13] although the origin of fibronectin is unclear. The gold standard for the diagnosis of malignant ascites is the presence of tumor cells in the ascetic fluid. Immunohistochemical staining combined with conventional cytologic examination increases the diagnostic sensitivity.[12]

Management

Management of patients with ascities in GI malignancies is controversial. There are different approaches to the treatment of malignant ascites, ranging from symptomatic relief with simple drainage procedures to chemotherapy and debulking surgery aimed at treating the underlying cancer. QoL and possibly the survival of patients with malignant ascites may be improved with the increasing availability and use of appropriate and potent combination chemotherapy.[14] The onset and progression of malignant ascites is associated with deterioration in QoL and a poor prognosis.[14] There are, however, no generally accepted evidence-based guidelines for evaluation and treatment of this condition. There are also no clinical predictors that identify cancer patients who will develop this distressing entity; hence, there are no preventive measures for its development. Malignant ascites presents with a multitude of symptoms including abdominal distension, respiratory embarrassment and early satiety, swelling of limbs, impaired mobility, nutritional deficiencies and its effects, the management of which requires prompt yet effective relief of symptoms with an eye on reducing recurrence. A logical approach is to individualize treatment. The rationale in the management of malignant ascites involves consideration of survival and QoL issues. Palliative techniques play an important role in the reduction of symptoms, which bear a direct correlation to patient satisfaction and therapeutic choices.[14,15]

In a random sample of 80 physicians practicing in Canada, physicians were questioned on their use of different modalities in management of malignant ascites and preferences based on attitudes toward efficacy of various treatments.[14] The most commonly used means of managing malignant ascites was paracentesis, which was also felt to be the most effective by the group surveyed. After paracentesis, diuretics and peritoneovenous shunting were used most frequently, but there was no apparent consensus as to their effectiveness.[14] A survey by Lee and colleagues showed that paracentesis and diuretics were the most commonly used procedures in management of malignant ascites followed by peritoneovenous shunts, diet measures and other modalities like systemic or intraperitoneal chemotherapy.[15] Symptom-based questionnaires have helped in evaluating the symptomatology and effectiveness of abdominal paracentesis.[15] Commonly used ones include the Edmonton Symptom Assessment System-Ascites Modification (ESAS:AM), the Memorial Symptom Assessment Scale-Short Form, the European Organization for the Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire (QLQ-C30), and the EORTC Core Quality of Life Questionnaire, 26-item pancreatic cancer module (QLQ-PAN26).[15] Most patients (78%) report that their symptoms improve after paracentesis (Table 4).

Subscales that included the most distressing symptoms were most responsive.[15] The amount of fluid removed (median, 3.5 L; range, 0.3 L to 9.7 L) did not correlate with symptom improvement (r=.29, P=–.10). All questionnaires showed strong sensitivity, validity and reliability. It has been suggested that for future clinical trials of symptomatic ascites, the QLQC30 and the ESAS:AM together, or the QLQ-C30 with the addition of the QLQ-PAN26 ascites and abdominal pain subscales could be used.[16]

Diet

Low sodium diet is the first step towards the management of ascites. It is believed to reduce the associated water retention and help reduce edema. Long-term sodium restriction has been shown to reduce recurrences and prolong the symptom-free period.[17]

Diuretic therapy

There are no randomized controlled trials assessing the efficacy of diuretic therapy in malignant ascites. Diuretic use in managing malignant ascites is inconsistent among physicians. A survey by Lee and colleagues showed that diuretics were used by 61% of physicians treating malignant ascites (27/44), but was felt to be effective by only 45% (20/44).[18] Phase II data suggest that the efficacy of diuretics in malignant ascites depends on plasma renin/aldosterone concentration.[19] In a study by Greenway and colleagues,[20] 13 of 15 patients responded to spironolactone (doses varying from 150 to 450 mg) and plasma renin activity was raised in all of 5 patients in whom it was measured (Table 5).

The SAAG gradient could serve as a guideline to

Table 1. Grades of ascites.

Severity	
Grade 1 (mild)	Not clinically evident, diagnosed on ultrasound
Grade 2 (moderate)	Proportionate sensible abdominal distension
Grade 3 (severe)	Noticeable tense distension of abdomen
Uncomplicated[8]	Not infected or associated with HRS
Refractory[9]	Cannot be mobilized, early recurrence after LVP, not prevented satisfactorily with medical treatment (after 1 week)
Diuretic-resistant	No response to intensive diuretic treatment
Diuretic-intractable	Drug-induced adverse effects preclude diuretic treatment

Table 2. Analysis of ascitic fluid.

Routine tests	Optional tests	Unusual tests
Cell count and differential	Glucose concentration	Tuberculosis smear and culture
Albumin concentration	LDH concentration	Cytology
Total protein concentration	Gram stain	Triglyceride concentration
Culture in blood culture bottles	Amylase concentration	Bilirubin concentration

Table 3. Classification of ascites by serum albumin ascites gradient.

High albumin gradient (SAAG >1.1)	Low albumin gradient (SAAG <1.1)
Cirrhosis	Peritoneal carcinomatosis
Alcoholic hepatitis	Peritoneal tuberculosis
Congestive heart failure	Pancreatitis
Massive hepatic metastasis	Serositis
Constrictive pericarditis and Budd-Chiari syndrome	Nephrotic syndrome

Table 4. Improvement following paracentesis.

Symptom	Improvement score (%)
Abdominal bloating	42-54
Anorexia	20-37
Dyspnea	33-43
Insomnia	29-31
Fatigue	14-17
Mobility	25

Table 5. Diuretics: Mode of action and toxicity profile.

Diuretic class	Examples	Mechanism of action	Site of action	Side effects
Loop diuretics	Furosemide, bumetanide, torsemide, ethacrynic acid	Inhibit sodium reabsorption at the Na-Cl-2K carrier	Medullary and cortical aspects of the thick ascending limb	Hypovolemeia, Hponatremia, Hypokalemia, Hypochloremia, Hypocalcemia, Hypomagnesemia, Metabolica alkalosis, teratogenicity
Thiazide diuretics	Hydrocholorthiazide, chlorthalidone, amiloride	Inhibit NaCl reabsorption in Na-Cl cotransporter and, to a lesser degree, parallel Na-H and Cl-HCO3 exchangers	Distal tubule the connecting segment at the end of the distal tubule	Hypokalemia, Hypochloremia, Hypomagnesemia, Hypercalcemia
Potassium-sparing diuretic	Amiloride, triamterene spirinolactone, eplerenone	Inhibit sodium entry through the aldosterone sensitive sodium channels (Na-K-H+ exchange)	Principal cells in the cortical collecting tubule (and possibly in the papillary or inner medullary collecting duct	Gynaecomastia, Hyperkalemia, Endocrine abnormalities.
Carbonic anhydrase inhibitors	Acetazolamide, dorazolamide	Inhibits activity of carbonic anhydrase	Proximal tubular cells.	Metabolic acidosis, neuropathy
Osmotic diuretic	Mannitol	A non-reabsorbable polysaccharide that acts as an osmotic diuretic, inhibiting sodium and water reabsorption	Proximal tubule and more importantly, the loop of Henle	Hypovolemia, dehydration

Table 6. Differences between paracentesis and peritoneovenous placement.

	Paracentensis	Peritoneovenous placement
Abdominal girth	No significant decrease	Significant decrease
Hematocrit	No significant decrease	Significant decrease
Blood urea nitrogen, creatinine	No significant change	Tended to decrease
Median no. of procedures	Two	One (P<.0001)
Postoperative performance score	No significant improvement	Significant improvement (P=.0026)
Median survival	18 days	42 days (P=.003)
Discharge rates	Lower	Higher (P=.0076)
Severe complications	Seven patients	One patient

determine response to diuretic therapy. In the prospective study by Pockros and colleagues,[19] a response to diuretics was seen in patients with ascites due to massive hepatic metastases who had a serum-ascites albumin gradient >1.1 g/dL (congruent to the serum-ascites albumin gradient of patients with benign ascites due to liver cirrhosis), whereas patients with ascites caused by peritoneal carcinomatosis or chylous malignant ascites who had no portal hypertension and a serum-ascites albumin gradient <1.1 g/dL did not respond to diuretics.

Paracentesis

Available data show good, although temporary relief of symptoms related to the build-up of fluid in about 90% of patients managed by paracentesis. There is no consensus on fluid withdrawal speed. Several durations have been reported, varying from 30-90 min[21] to 19-24 hours.[22] Possible complications of paracentesis include secondary peritonitis, pulmonary emboli and hypotension.[23] Fischer reported about 300 cases of abdominal paracentesis for malignant ascites where 5% dextrose was infused intravenously simultaneously and no episodes of severe hypotension were recorded.[24] Endoscopic ultrasound-guided paracentesis (EUS-P) is highly sensitive and specific for diagnosing malignant ascites.[24] The finding of malignant ascites significantly alters patient management, so an active search for ascites and use of EUS-P should be incorporated into the diagnosis and staging of upper GI and pancreaticobiliary tumors.[24] The sensitivity, specificity, positive predictive value, and negative predictive value of EUS-P for diagnosing malignant ascites was 94%, 100%, 100%, and 89%, respectively.[25] Studies in the context of liver disease showed that up to 5 L can be removed quickly without risk of significantly affecting plasma volume or renal function.[26-28] Stephenson and colleagues retrospectively analyzed 30 paracenteses in 12 patients with malignant ascites after implementing a guideline allowing up to 5 L fluid to drain without clamping and giving intravenous fluids only when specifically indicated. In the analyzed 30 paracenteses, intravenous fluids or blood products were given only in 6 procedures and there was no case of symptomatic hypotension.[29]

McNamara did a prospective study in the context of malignant ascites, observing 48 paracenteses in 44 patients to evaluate how much fluid needs to be drained for symptom relief. The results suggest that a significant improvement of the symptoms of abdominal pressure occurs with the removal of few liters (range 0.8-15 L, mean 5.3 L, median 4.9 L).[30] There are no randomized trials comparing paracentesis with the use of diuretics in the management of malignant ascites. A phase II study suggests that installation of Iscador M (visucs albumin extract) into the peritoneal cavity may reduce the need for repeated punctures.[31] This offers significant hope for patient compliance given the nature of recurrence of ascites and the resultant frequent hospital visits.

Peritoneovenous shunts

There are two main types of peritoneovenous shunt (PVS) systems, the Le Veen shunt[32] and the Denver shunt.[33] The Le Veen shunt drains ascitic fluid into the superior vena cava by a one-way valve opening at a pressure of 3 cm of water. With the Denver shunt, the valves open at a positive pressure gradient of about 1 cm of water, preventing reflux. There have been no prospective randomized studies comparing the patency rates of the two systems in malignant ascites.[34] Souter and colleagues evaluated 43 patients with malignant ascites, 16 receiving a Denver Shunt, 27 receiving a Le Veen shunt. They observed that shunt occlusion was more common with the Denver Shunt, but the two groups of patients were not selected at random and therefore may not be comparable.[35] LeVeen and Denver peritoneovenous shunt complications other than patency are comparable. The Le Veen is preferred for its superior patency in cirrhotic patients with intractable ascites. Hemorrhagic ascites and ascitic fluid protein content greater than 4.5 g/L are considered contraindications for shunting because of the higher risk of shunt occlusion.[35] Loculated ascites, portal hypertension, coagulation disorders and advanced cardiac or renal failure are also contraindications.[35] Although clinical observations and findings at necropsy indicate that peritoneovenous shunting does not result in the establishment of clinically important hematogenous metastases,[36] some studies have shown that tumor cells infused into the central venous system can lead to massive early metastases.[37] Reported median survival of patients with malignant ascites varies between 52 and 266 days,[34] indicating that patient selection assumes paramount importance in deciding upon further management. In all reported studies, patients with ovarian and breast cancer who undergo peritoneovenous shunting have the best response rate (>50%) whereas the response rate in patients with gastrointestinal cancers is far worse (10% to 15%).[37] Because of poor prognosis, it is agreed by most authors that shunt insertion is contraindicated in patients with malignant ascites due to gastrointestinal cancer.[14] An insertion of a shunt is associated with potentially fatal side-effects and costs in terms of time and money, considering that patients need to be monitored closely for at least 24 hours after operation with a central venous pressure line to monitor fluid balance. Therefore a shunt should only be used when other treatment options like diuretics have failed and when the life expectancy of the patient is long enough to derive benefit. There is no consensus on the time span; some authors advocate more than one month,[38] while others suggest an expected survival of more than 3 months.[39,40] The use of shunts has to be balanced by the potential risks of this procedure.

Tenckhoff catheter

This catheter is surgically placed through the wall of the abdomen to provide a point for the dialysis solution to enter and leave the peritoneal cavity during peritoneal dialysis.[41] It provides good access to the peritoneal cavity for chronic peritoneal dialysis and treatment of intraperitoneal malignancy. There are various methods for placement like blind insertion, open surgical implantation and peritoneoscopic guided placement. Ultrasound guidance is used for safe insertion. Infection is a frequent complication. Contraindications are peritonitis and sepsis.

Paracentesis vs PVS placement

There is no difference in survival or quality of life between patients treated with repeated abdominal paracentesis and patients treated with a PVS.[32] In one study, 20 patients underwent PVS placement and 49 patients were subjected to paracentesis (Table 6). PVS placement thus provides an effective treatment option for patients with refractory malignant ascites in advanced cancer, and yields a higher likelihood of discharge compared with conventional paracentesis.[42]

Image-guided biopsies

When used in the context of multidisciplinary team discussion, image-guided biopsy using ultrasound (US) or computed tomography (CT) guidance is of value in planning the management of women with suspected ovarian cancer and peritoneal carcinomatosis (PC) of uncertain etiology.[42] It is essential in women believed to have ovarian cancer, but with poor performance status or with advanced disease believed beyond the scope of primary cytoreductive surgery for which staging surgical pathology will not be obtained. It provides a site-specific primary tumor diagnosis in 93% of cases and should replace diagnostic laparoscopy or laparotomy for this purpose.[43] The technique is simple, safe and effective and can be combined with palliative drainage of ascites at the same procedure.[43]

Recommendations

Although abdominal paracentesis, diuretics and peritoneovenous shunting are commonly used procedures in management of malignant ascites, the evidence for these treatment options is weak. There are no randomized controlled trials evaluating the efficacy and safety of these procedures in malignant ascites. Available data show a good but temporary effect of abdominal paracentesis on symptom relief in patients with malignant ascites. There is no consensus on fluid withdrawal speed and concurrent intravenous hydration is not sufficiently studied. Data show that peritoneovenous shunts can control malignant ascites, but have to be balanced by the potential risks of this procedure. The use of diuretics should be considered in all patients, but has to be evaluated individually. A recommendation for further research is a randomized controlled trial comparing the use of diuretics with paracentesis in the management of malignant ascites.[34] Guidelines in the management of symptomatic malignant ascites in advanced cancer. Paracentesis is indicated for those patients who have symptoms of increasing intra-abdominal pressure. Available data show good, although temporary relief of symptoms in most patients. Symptoms like discomfort, dyspnea, nausea and vomiting seem to be significantly relieved by drainage of up to 5 L of fluid. When removing up to 5 L of fluid, intravenous fluids seem to be not routinely required (grade of recommendation: D) (Grading of the evidence and the recommendations in the guideline are based on the revised grading system by the Scottish Intercollegiate Guidelines Network (SIGN). Grades of recommendations are from grade A to D. Grade A: At least one meta-analysis, systematic review, or RCT rated as 1++ and directly applicable to the target population. Grade B: A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results. Grade C: A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results. Grade D: Evidence level 3 or 4 or Extrapolated evidence from studies rated as 2+).[44] If patient is hypotensive or dehydrated or known to have severe renal impairment and paracentesis is still indicated, intravenous hydration should be considered. Infusion therapy is not sufficiently studied. The only investigated therapy in malignant ascites is infusion of dextrose 5%. There is no evidence of concurrent albumin infusions in patients with malignant ascites (grade of recommendation: D). To avoid repeated paracenteses, peritoneovenous shunting may be considered. Major complications (pulmonary edema, pulmonary emboli, clinically relevant disseminated intravascular coagulation and infection) have to be expected in about 6% of patients (grade of recommendation: D). There are no randomized controlled trials assessing the efficacy of diuretic therapy in malignant ascites. The available data are controversial and there are no clear predictors to identify which patients would benefit from diuretics. The use of diuretics therefore should be considered in all patients, but has to be evaluated individually. Patients with malignant ascites due to massive hepatic metastasis seem to respond more likely to diuretics than patients with malignant ascites caused by peritoneal carcinomatosis or chylous ascites (grade of recommendation: D).[32]

Newer pharmacological approaches in the management of malignant ascites

Intraperitoneal Immunotherapy

Interferon alpha

One study reported that there was resolution of malignant ascites in 3 of 10 patients treated with intraperitoneal interferon alpha-2b.[45] Another study showed a 36% complete response and 9% partial response with intraperitoneal administration of interferons in patients with ovarian cancer.[46] The only significant frequently occurring side effect was pyrexia. No significant myelosupression was observed.[46] Parenteral interferon has also shown to give positive results in one small study in which intramuscular interferon was given to 5 patients with advanced ovarian carcinoma.[47] Ascitic fluid production stopped in 2 patients, while disease remained stable in more than 1 year in 2 others and was improved in the fifth patient.

Tumor necrosis factor-alpha

Tumor necrosis factor (TNF)-alpha has been shown to be effective in the palliative treatment of malignant ascites.[48] One study showed a good response to TNF-alpha therapy in patients with malignant ascities. Of 22 patients, 16 had complete and 6 had partial resolution of their ascites. The response rate was highest in patients with ovarian cancer in which the tumor load was distributed in fine nodules all over the peritoneal cavity rather than as palpable bulky masses characteristic of non-ovarian tumors. Some reversible adverse affects such as fever, chills, nausea, vomiting, and fatigue were reported, but these were generally well tolerated.

OK-432

A large Japanese study showed favorable results in the use of intraperitoneal injections of streptococcal antigen OK-432 in patients with malignant ascites.[49] Of 200 patients with malignant ascites of gastrointestinal malignancies, 150 were randomly selected to be administered 6 intraperitoneal injections of OK-432 at intervals of 1 week, while the remaining 50 patients served as control subjects. Of the 150 treated patients, 76 had a complete response (inability to drain any fluid) and 8 had a partial response (decrease in abdominal girth of >10 cm), giving a total response of 56%. Furthermore, the OK-432 group had a better survival time (10.2 months) compared with the control group (3.1 months). Although each of the above studies had limitations, they suggest that intraperitoneal immunotherapy may have a role in the future management of malignant ascites.

Anti-VEGF therapy

Decreasing permeability of vessels by inhibiting the tyrosinase kinase activity of vascular endothelial growth factor (VEGF) receptors has recently been shown to inhibit the formation of malignant ascites in animal models.[50] In that study, the tyrosine kinase inhibitor PTK 787 was evaluated in 2 ovarian cancer cell types. Hey-A8 cells express low levels of VEGF and grow as solid tumor foci on the surface of peritoneal organs, whereas SKOV3 i.p.1 cells express high levels of VEGF and grow as peritoneal tumors and ascites. Treatment of nude mice by means of daily oral administration of 50 mg/kg of PTK 787 was not effective against Hey A-8 tumors, but significantly inhibited the growth of SKOV3 i.p.1 cells and the formation of malignant ascites. Furthermore, survival was increased in SKOV3 mice.[51] These findings suggest that blockage of the VEGF/vascular permeability factor receptor may be a useful strategy for inhibiting the formation for malignant ascites. This conclusion is further supported by a second study in mice using VEGF-neutralizing antibodies.[51] Human studies will now be required to test this potentially promising approach toward the management of malignant ascites.

Metalloproteinase inhibitors

Encouraging results have also been reported with the intraperitoneal instillation of the metalloproteinase Batimastat.[52] Twenty three patients with malignant ascites had Batimastat instilled into the peritoneal cavity after paracentesis. No reaccumulation of ascites occurred after that single dose in 5 of the 23 patients, and these 5 survived for up to 112 days. Seven other patients died without reaccumulation. Nausea and vomiting were noted in the first 24 hours after batimastat treatment, but overall tolerance was good, and no significant acute peritoneal reactions were reported. Opposite results, however, were obtained in an animal study in which treatment caused dramatic tumor cell consolidation and less dispersed ascites cells compared with controls, but did not reduce ascites.[53] It is thus suggested that larger, controlled trials will be necessary before metallopreoteinase inhibitors can be recommended for routine clinical use.

Radioimmunotherapy

Recently, monoclonal antibody therapy has been used in treating malignant ascites with some success. Five patients with colon or ovarian cancer or mesothelioma were treated with intraperitoneal monoclonal antibody radiolabelled with 131I.[53] Three of the four assessable patients had resolution of ascites for a mean of 4 months, such that no further paracentesis or diuretic therapy was required. A phase I/II study using a novel anti-mucin monoclonal antibody 2G3 labelled with 131I12 was conducted on 11 patients with chemo-resistant ascites, secondary to ovarian or breast cancer.[54] The radioimmunotherapy was given by intraperitoneal injection and in three of the four patients who received the highest doses temporary palliation of their ascites lasting 6 weeks to death at 4 months was reported.

Octreotide

Octreotide, a somatostatin analogue, has been used in the symptomatic management of bowel obstruction, uncontrolled diarrhea and fistulae. It decreases the secretion of fluid by the intestinal mucosa, and increases water and electrolyte reabsorption.[55] In a study of this agent given subcutaneously in doses ranging from 200 to 600 mcg/24 h to three patients with metastatic adenocarcinoma and ascites, Cairns found that two had a reduction in ascites such that further paracentesis was not required.[55] More evidence is needed for the establishment of its efficacy in malignant ascites.

Conclusion

Ascities is a common finding in gastrointestinal malignancies. The effective management of ascities is necessary in treating the symptoms of these patients. We most use ascitic fluid drainage as the most common intervention. Other treatment modalities are specific for the type of malignancies present in the body. Radio- and immunotherapy and other anti-tumor therapies have been used, but none are fully successful in the management of ascites in these patients.

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brief report

Vitamin D levels in healthy men in eastern Saudi Arabia

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Ann Saudi Med 2009; 29(5): 378-382

BACKGROUND: Studies in 1980s and 1990s indicated that vitamin D levels in the ethnic Saudi Arabian population were low but no studies since that time have evaluated vitamin D levels among healthy young or middle-aged Saudi men. Thus, we assessed the serum level of 25-hydroxyvitamin D (25OHD) among healthy Saudi Arabian men living in the Eastern Province.

SUBJECTS AND METHODS: One hundred males aged 25-35 years (the age range of peak bone mass) and 100 males aged 50 years or older were randomly selected and evaluated clinically, including measurement of serum calcium, parathyroid hormone (PTH) and serum 25OHD levels. Vitamin D deficiency was defined as a serum level of 25OHD of ≤20 ng/mL and insufficiency as a serum level between >20 ng/mL and <30 ng/mL and normal ≥30 ng/mL.

RESULTS: The mean (SD) age of subjects in the younger age group was 28.2 (4.5) years. Twenty-eight (28%) had low 25OHD levels; 10 (10%) subjects were vitamin D deficient with a mean level of 16.6 (3.4) ng/mL and 18 (18%) were vitamin D insufficient with a mean level of 25.4 (2.7) ng/mL. In the older age group, the mean age was 59.4 (15.6) years and 37 (37%) had low 25OHD; 12 (12%) subjects were deficient with a mean 25OHD level of 16.7 (3.4) ng/mL and 25 (25%) were insufficient with a mean 25OHD level of 25.3 (3.3) ng/mL.

CONCLUSIONS: The prevalence of vitamin D deficiency among healthy Saudi men is between 28% to 37%. Vitamin D deficiency among young and middle age Saudi Arabian males could lead to serious health consequences if the issue is not urgently addressed.

The two main forms of vitamin D are vitamin D2 or ergocalciferol, which is obtained from plant and foods such as mushrooms, fish and egg yolk, and vitamin D_3 or cholecalciferol, which is formed in the skin after exposure to sunlight or ultraviolet light. Vitamin D is important for calcium homeostasis and essential for skeletal health. Deficiency of vitamin D is responsible for the development of rickets in children and osteomalacia in adults.[1] There is no absolute consensus on the cut-off value between a normal and low level of vitamin D. Recently, many studies have used 32 ng/mL as a cut-off value and most experts now recommend the normal level of 25-hydroxyvitamin D (25OHD) to be ≥30 ng/mL. They have also agreed to define vitamin D insufficiency as a level of >20-29 ng/mL and deficiency when the level is ≤20 ng/mL.[2] There are many causes of vitamin D deficiency, which are related to decreased synthesis, deceased bioavailability, increased catabolism or demands and increased urinary loss. It has been estimated that around one billion persons worldwide have vitamin D deficiency or insufficiency.[3] Saudi Arabia is one of the sunniest areas of the world and exposure to sunlight might be assumed to be sufficient to maintain adequate vitamin D status. However, vitamin D deficiency is common among the Saudi population. As early as 1982 Woodhouse and Norton[4] reported low vitamin D levels in the ethnic Saudi Arabian population. Later, Sedrani and colleagues confirmed the earlier finding,[5] and also found that low vitamin D levels were not related to one region, sex, age or season.[6] Despite these reports no action was taken to adequately fortify foods or encourage people to increase their vitamin D intake. Recent attention to the high prevalence of osteoporosis and its association with low vitamin D levels in adults has raised the importance of vitamin D evaluation. In addition to many other risk factors, a low level of vitamin D is considered to be one of the most important risk factors for osteoporosis and related fractures.[7,8] Chapuy[9] reported that adequate vitamin D intake can prevent hip fractures while Lips et al[10] have shown that vitamin D is essential for calcium metabolism as well as for fracture prevention. In the last 3 to 4 decades the dietary habits and lifestyle of children and adults in Saudi Arabia has changed tremendously,[11] but vitamin D levels among Saudis have not been reassessed. To our knowledge, no recent studies have evaluated vitamin D levels among healthy young or middle-aged Saudi men. This objective of this study was assessment of serum 25OHD levels among healthy Saudi males.

SUBJECTS AND METHODS

This cross-sectional study was carried out over a 3-month period between 1 February 2008 and 31 May 2008 at King Fahd Hospital of the University-Al Khobar, located in the Eastern Province of Saudi Arabia. The study was approved by the research and the ethical committee of the Medical College at King Faisal University, Dammam. Two hundred healthy Saudi Arabian men were randomly selected, including 100 males aged 25 to 35 years (the age range of peak bone mass) and 100 males aged 50 years or older. Exclusion criteria were the presence of chronic diseases that affect vitamin D status such as malabsorption, chronic liver disease, renal impairment or nephritic syndrome, the use of vitamin D supplements, or drugs that can affect vitamin D metabolism such as anticonvulsants or corticosteroids, and a family history of hypocalcemia or vitamin D disorders. Informed verbal consent was obtained from all the candidates. Demographic data such age and sex in addition to information on sunlight exposure for the purpose of obtaining vitamin D and the frequency and amount of dairy product consumption were obtained through a questionnaire. Subjects 25 to 35 years of age were recruited from medical students, interns, and residents in addition to hospital employees. Men aged 50 years and older were randomly selected from visitors to the hospital and examined clinically to rule out the presence of any disease of exclusion. Blood samples were taken from all subjects in the morning and after an overnight fast. Samples were kept frozen at -20°C until the time of analysis. Serum calcium, serum phosphorous, alkaline phosphatase and parathyroid hormone levels were determined by standard laboratory procedures. Serum levels of 25-hydroxyvitamin D3 (25OHD3) were measured by radioimmunoassay using the Wallac 1470 Gamma Counter (Wallac Inc, Gaithersburg, MD, USA). 25OHD3 were considered normal if >30 ng/mL. Vitamin D deficiency was defined as a serum level of 25OHD of ≤20 ng/mL and insufficiency as a serum level between >20 ng/mL and <30 ng/mL. The data were analyzed using SPSS (Statistical Package for the Social Sciences), version 14.0, Chicago, Illinois. Data were expressed as the mean and standard deviation. Statistically significant differences between groups were determined with the t test. *P* values of less than .05 ($P<.05$) using a confidence interval (CI) of 95% were considered significant.

RESULTS

In the men aged 25 to 35 years, 72 (72%) had a normal level of 25OHD3 and 28 (28%) had a low level, of whom 18 (18%) were insufficient and 10 (10%) were deficient (Table 1). The mean age of subjects in the three groups were similar. In the men aged 25 to 35 years, the mean levels of the 25OHD3 were significantly lower in the subjects who were insufficient and deficient as compared to the normal subjects. When compared to normal subjects, serum calcium was significantly lower in insufficient subjects ($P=.002$) whereas alkaline phosphatase and parathyroid hormone levels were higher in deficient subjects, though they were still within the normal range. Fifteen patients in the three groups consumed dairy products equivalent to about 250 mL of milk per day and there was no statistically significant difference between the groups. Only 6 patients reported exposure to sunlight for the sake of obtaining vitamin D. For subjects aged 50 years and older, sixty-three (63%) had normal 25OHD3 levels while levels were low in 37 subjects (37%) (Table 2). Of those with low 25OHD3 levels, 25 (25%) were insufficient and 12 (12%) were deficient. Mean levels of 25OHD3 were significantly different between the three groups. Deficient subjects were older than normal subjects ($P=.001$). Alkaline phosphatase was significantly higher in insufficient and deficient subjects and parathyroid hormone levels, though in the normal range, were higher in insufficient and deficient subjects when compared to normal subjects ($P=.002$). Few patients in this age group consumed dietary products or exposed themselves to sunlight.

DISCUSSION

There are many risk factors for vitamin D deficiency.[3] Rickets, which is predominately related to vitamin D deficiency, was highly prevalent during the early twentieth century when more than 80% of children living in industrialized cities in Europe and North America suffered from the disease,[3] After the initiation of food-fortifying programs, it was assumed that vitamin D

Table 1. Clinical and demographic data for healthy men aged 25-35 years (n=100).

	Normal 25OHD (≥30 ng/mL) (A)	25OHD insufficiency (>20-<30ng/mL) (B)	25OHD deficient (≤20 ng/mL) (C)	*P* between A and B	*P* between A and C
Number of subjects	72	18	10		
Mean (SD) age (years)	27.9 (3.5)	28.9 (4.3)	28.5 (4.5)	.1	.1
Exposure to sunlight (min/day)	5	0	1	.01	.01
Adequate consumption of dairy products (250 mL/day)	9	2	4	.8	.02
Calcium level (mg/dL) (normal, 8.5-10.5)	9.5 (0.6)	9.1 (0.3)	9.2 (0.5)	.002	.3
Phosphorus (mg/dL) (normal, 2.5-4.9)	3.9 (0.6)	3.6 (0.4)	3.7 (0.7)	.1	.1
Alkaline phosphatase (IU/L) (normal, 50-140)	87.6 (31.7)	85.9 (17.9)	105.5 (16.2)	.2	.01
Parathyroid hormone (pmol/L) (normal, 1.3-7.6)	5.0 (2.2)	5.2 (1.5)	6.9 (2.7)	.1	.06
25-hydroxyvitamin D3 (ng/mL) (normal, >30 ng/mL)	43.8 (6.4)	25.4 (2.7)	16.6 (3.4)	.01	.01

Values are mean (standard deviation) unless noted otherwise.

Table 2. Clinical and demographic data for healthy men aged 50 years or older (n=100).

	Normal 25OHD (≥30 ng/mL) (A)	25OHD insufficiency (>20-<30 ng/mL) (B)	25OHD deficient (≤20 ng/mL) (C)	*P* between A and B	*P* between A and C
Number of subjects	63	25	12		
Mean (SD) age (years)	58.7 (8.1)	58.3 (9.7)	64.8 (15.7)	.2	.001
Exposure to sunlight (min/day)	9	2	3	.1	.4
Adequate consumption of dairy products (250 mL/day)	12	3	2	.8	.4
Calcium level (mg/dL) (normal, 8.5-10.5)	9.0 (0.7)	9.2 (0.3)	9.1 (0.2)	.9	.3
Phosphorus (mg/dL) (normal, 2.5-4.9)	3.8 (0.5)	3.9 (0.6)	3.5 (0.2)	.2	.3
Alkaline phosphatase (IU/L) (normal, 50-140)	87.1 (32.4)	84.8 (26.3)	109.5 (19.2)	.1	.001
Parathyroid hormone (pmol/L) (normal, 1.3-7.6)	5.2 (3.4)	5.7 (0.6)	6.4 (0.7)	.1	.002
25-hydroxyvitamin D3 (ng/mL) (normal, >30 ng/mL)	39.8 (5.9)	25.3 (3.2)	16.7 (3.4)	.001	.001

Values are mean (standard deviation) unless noted otherwise.

deficiency was eradicated and no longer a health issue in Western and developed countries.[12] However, recent reports indicate that vitamin D deficiency is still rampant, especially among the elderly and it continues to be an unrecognized epidemic in many populations worldwide.[12] Dharmarajan et al[13] reported that 54% of their patients had suboptimal vitamin D levels. In general, the prevalence of vitamin D deficiency (<20 ng/mL or 50 nmol/L) in otherwise healthy young adults 18 to 29 years is 36% and it is much higher among black women, elderly people and general medicine inpatients.[14] Vitamin D deficiency has many health consequences. It has long been recognized that both insufficiency and deficiency of vitamin D can cause serious effects on the skeleton and other systems.[12,15]

This study from the eastern region of Saudi Arabia raises a concern of a health issue for the Saudi population at large. Twenty-eight percent of healthy men at the age of peak bone mass (25 to 35 years of age) and 37% of healthy men aged 50 years and older in this cross-sectional study were suffering from low vitamin D levels (insufficiency and deficiency). This prevalence is higher than the previously reported figure of 20% from the Eastern Province.[3] Also, this prevalence is much higher than what was reported by Atli et al,[16] who found vitamin D deficiency in only 15.3% of elderly males from Turkey. On the other hand, the prevalence of vitamin D deficiency among our subjects was lower than that reported recently by O'Sullivan et al[17] who found low 25OHD levels in 54% of their healthy young men with an average age of 36 years. Very low vitamin D levels have been reported from other Middle Eastern countries, particularly from Lebanon, Iran, Jordan and Turkey.[18-20]

Of great concern is the finding that 28% of healthy men aged 25 to 35 years had low 25OHD. Vitamin D is essential for the attainment of adequate peak bone mass and it plays a key role in bone development and bone density. Not reaching the expected peak bone mass at this age may predispose subjects to the development of osteopenia and osteoporosis at a later age.[21] This can partially explain our previous finding of a high prevalence of osteopenia and osteoporosis among Saudi men older than 50 years of age.[22] In the current study, a low vitamin D level was found to be prevalent among our healthy subjects older than 50 years and as expected, the mean age of patients with deficiency was older than that of patients with a normal vitamin D level. This finding should alert us to the importance of proper and adequate supplementation of vitamin D when treating patients with osteopenia or osteoporosis.[10] Despite the presence of low vitamin D among subjects in both age groups, serum calcium and parathyroid hormone were in the normal range, which supports the importance of assessment of vitamin D levels if clinically indicated.[23] Although our subjects were healthy and active and despite the fact that Saudi Arabia is one of the sunniest countries, with sun available most days throughout the year, few patients in either age group had sensible sunlight exposure for the sake of obtaining vitamin D, which is considered the main source of vitamin D.[24] Avoidance of sunlight might be a contributing factor to the high prevalence of low vitamin D in our population. The cultural practice of wearing long sleeves and head covers that also cover part of the face is unlikely to be the major cause of vitamin D deficiency among our subjects. In fact Sedrani et al[5] found adequate serum 25OHD levels among Saudi female students who were veiled and more extensively clothed. The finding of Sedrani et al[5] stresses the importance of public education about the importance of making time for sun exposure for the sake of obtaining vitamin D. On the other hand, only 15% of the younger group and 17% of the older group consumed an adequate amount of dairy products, which again indicates a lack of public awareness about the importance of adequate calcium intake.

The time of year is an important factor in measurement of vitamin D levels in the diagnosis of insufficiency or deficiency. Bolland et al[25] found that summer is the ideal time to measure vitamin D levels as there is seasonal variation with a 14% increase 25(OH) D concentrations in men in the summer,[26] but Saadi et al[27] found that mean serum 25OHD was highest in April, which marks the end of the winter season. We measured the 25OHD in the spring/summer season, which could have been the highest level of 25OHD3.

Our study has a few limitations. The study sample of 200 healthy individuals was small and the fact that blood samples were collected only once during the months of February to May. It would be useful if patients were evaluated at different times of the year to study the seasonal variation. Also the Eastern Province of Saudi Arabia is located on the coast of the Arabian Gulf and high fish consumption would be expected, but unfortunately, this information was not collected from the subjects.

In conclusion, even though not representative of all Saudi men living in the country, our study suggests that low vitamin D is prevalent in apparently healthy Saudi men. The deficiency of vitamin D might be related to lack of adequate exposure to sunlight and possibly inadequate consumption of dairy products. We believe that there is an urgent need for public education about the role of vitamin D in health to avoid the complications of vitamin D insufficiency and deficiency.

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brief report

Hepaticocholecystoduodenostomy compared with Roux-en-y choledochojejunostomy for decompression of the biliary tract

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Ann Saudi Med 2009; 29(5): 383-387

BACKGROUND AND OBJECTIVES: The nature of palliative decompressive surgery for unresectable periampullary tumor is usually determined by the experience of the surgeon. We compared hepaticocholecystoduodenostomy (HCD), a new palliative decompressive anastomotic technique, to Roux-en-y choledochojejunostomy (CDJ) in this prospective, randomized study.

PATIENTS AND METHODS: Twenty patients who were to undergo surgery for palliative bypass were randomized into two groups: group I was subjected to HCD (10 patients) and group II to CDJ (10 patients). Pre- and postoperative liver function tests, operative time, operative blood loss, onset of postoperative enteral feeding, length of hospital stay and survival rates were compared in the two groups.

RESULTS: Effective surgical decompression was observed clinically as well as on analysis of pre- and postoperative liver function tests in both the groups. The results were statistically significant in favor of patients in group I when compared to those of group II with respect to operative time 84.7 (10.3) min vs 133.6 (8.9) min; P=<.0001), operative blood loss 137.8 (37.2) mL vs 201.6 (23.4) mL; P=.001), postoperative enteral feeding 3.3 (0.5) days vs 5.0 (0.7) days; P=<.0001) and length of hospital stay 7.5 (0.7) days vs 9.7 (1.2) days ; P=<.0001). During follow-up, recurrent jaundice was observed in one patient in group I and two patients in group II, while duodenal obstruction developed in one patient in the group I series. Gastrointestinal hemorrhage occurred in one patient belonging to group II. The difference in mean survival time was not statistically significant.

CONCLUSION: Based on this small series, HCD seems to be a better palliative surgical procedure than the routinely performed CDJ.

Periampullary cancer may arise from the head of the pancreas, the ampulla of Vater, the lower part of the common bile duct or the duodenal mucosa. Often due to the late presentation of the disease, patients are subjected to palliative therapy with a view to relieve obstructive jaundice, gastric outlet obstruction and pain.[1-3] Operative and nonoperative modalities are currently available to provide reasonable palliation of symptoms. Appropriate palliative surgical management is indicated in patients found to have unresectable tumors at the time of laparotomy or those whose symptoms are not amenable to current nonoperative palliative techniques. Various surgical bypass procedures are performed for relief from obstructive jaundice. The most frequently used procedures are hepaticojejunostomy, cholecystojejunostomy, choledochojejunostomy and choledochoduodenostomy. To our knowledge hepaticocholecystoduodenostomy (HCD), a palliative decompression procedure has not been attempted in such cases. This study attempts to introduce the procedure of HCD as a decompressive procedure in such cases. HCD involves the interposition of the gallbladder between the common hepatic duct and the second part of duodenum to facilitate the free drainage of bile. In this study, we compared the outcome of this procedure (HCD) with the routinely performed choledochojejunostomy (CDJ) to assess the HCD as a new viable procedure for palliative decompression in unresectable cases of periampullary tumors.

PATIENTS AND METHODS

The patients included in this study had unresectable and histologically proven periampullary adenocarcinoma detected preoperatively (included patients with advanced disease where biliary stenting has failed or stents were repeatedly blocked) or intraoperatively by finding of fixed tumors non-amenable for palliative surgical bilioenteric bypass. These patients were enrolled in the Department of Surgical Gastroenterology at Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir, India, for this study, which extended from January 2004 to January 2008. The diagnosis of the tumor was based on clinical examination and was aided by ultrasonography (US), CT and endoscopic retrograde cholangiopancreatography (ERCP). Radiologically the criteria for determining resectability included the presence or absence of distant metastases and local invasion of the major retroperitoneal vascular structures, especially the portal and superior mesenteric veins and the superior mesenteric artery. Histological proof was obtained either by tissue biopsy on lateral duodenoscopy or by USG/CT-guided fine needle aspiration biopsy (FNA) of the tumor mass. Patients with a history of endoscopic biliary drainage, prior biliary surgery or gall stone disease were excluded from the study.

Randomization of patients was carried out intraoperatively based on random number allocation after the surgeon declared the tumor as unresectable. Patients were assigned HCD (group I), or CDJ (group II) by a technologist in the operating theatre after opening an opaque sealed envelope. Inclusion criteria were a dilated common bile duct, distended gallbladder, no tumor encroachment of the terminal cystic duct, no features of duodenal obstruction, and sufficient grounds to believe that either procedure would be technically safe. For comparison, relevant details including pre- and postoperative liver function test results, operative time, operative blood loss, onset of enteral feeding, length of hospital stay and survival rates were recorded in each group.

Surgical technique

Surgical exploration was performed using a right subcostal incision. Once the suitability of the patient for the procedure was ascertained, serosa of the hepatoduodenal ligament was opened and common hepatic and bile ducts exposed, whereupon the distended gallbladder (GB) was seen to lie close to the common hepatic duct (CHD) and the duodenum below. Hartmann pouch was mobilized to facilitate approximation of the CHD and the neck of GB, transfixation sutures were placed between the two structures (Figure 1) A 15-20 mm side to side anastomosis was performed between the CHD and neck of the GB by a single layer of interrupted sutures using 3-0 polyglycolic acid (Figure 2). While performing the anastomosis, due care was taken to avoid injury to the main cystic artery lying in the triangle between the CHD and the cystic duct (cystohepatic triangle). The fundus of the gallbladder was grasped with a noncrushing intestinal clamp and it was freed by careful dissection of the surrounding tissue; the duodenum was also freed from its lateral peritoneal attachments (the Kocher maneuver). A single layer interrupted two to three cm side to side cholecystoduodenostomy was performed in the second part of the duodenum on its anterior aspect well away and below the tumor (Figure 3). After placing a tube drain in Morison pouch, the abdomen was closed in layers. For choledochojejunostomy, the markedly distended GB was removed and a Roux-en-y loop of jejunum was prepared for the classical side to side choledochojejunostomy anastomosis. Bypass was considered a failure if reoperation or other therapeutic intervention was necessitated for managing postoperative complications related to biliary anastomosis or recurrence of jaundice. After leaving the hospital, patients were followed by direct or telephonic contact. The study was approved by the institute ethical committee, and informed consent was obtained from all the patients for participation in the study.

Summary statistics for quantitative data were the mean and standard deviation (SD) presented as "mean (SD)". Quantitative data between the two treatment

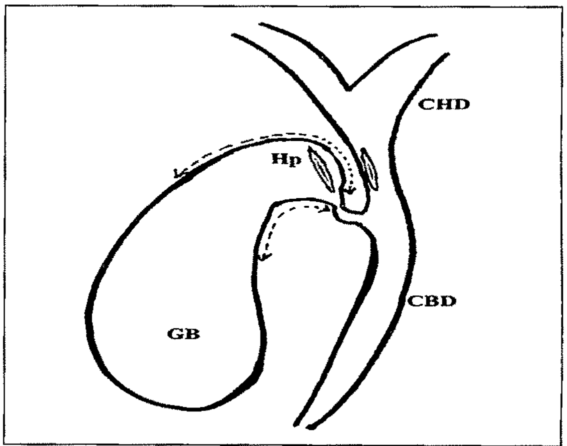

Figure 1. After mobilization (_-----_) of Hartmann's pouch (Hp) from liver bed, the distended common hepatic duct (CHD) and Hartmann's pouch are incised at a length of 15-20 mm. The incised parts are anchored by three transfixing sutures, A-a, B-b and C-c (See figure 2). CHD-Common hepatic duct, Hp-Hartmann pouch, GB-Gallbladder. CBD-Common bile duct.

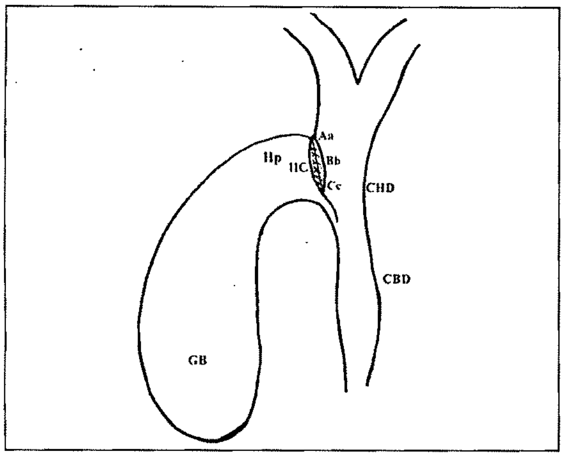

Figure 2. Anastomosis between gallbladder (GB) and the common hepatic duct (CHD) performed by a single layer interrupted 3-0 polyglcolic acid sutures. A-a, B-b and C-c, transfixing sutures in place. HC- Hepaticocholecystostomy.

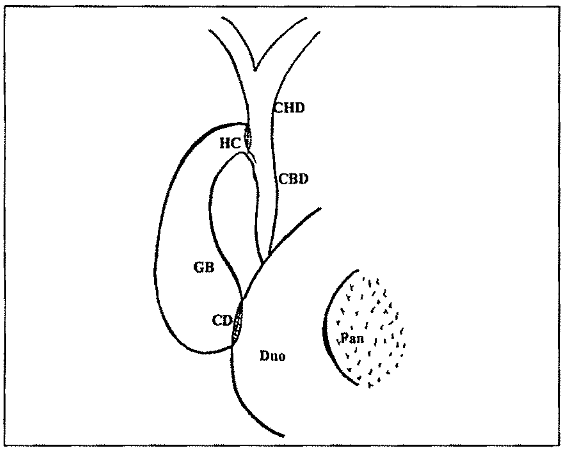

Figure 3. A side-to-side cholecystoduodenostomy (CD) is performed by interrupted 3-0 polyglcolic acid sutures. HC-Hepaticocholecystostomy, GB-Gallbladder, CD-Cholecystoduodenostomy, Duo-Duodenum, CHD-Common hepatic duct, CBD-Common bile duct, Pan-Pancreas, Hp-Hartmann pouch.

groups was compared using the t test for parametric data. All P values were two-tailed; P values less than .05 were considered statistically significant. Statistical analysis was performed using a statistical software program (SPSS 11.5.0)

RESULTS

Each group had 10 patients with the mean patient age in group I (HCD group) being 64.1 years (range, 56-72 years) and group II (CDJ group) 61 years (range, 50-72 years). There were 6 females and 4 males in group I, 7 males and 3 females in group II. The chief complaints of patients in either group were itching, jaundice and pain. Preoperatively, USG and CT were useful in detecting advanced lesions in 7 patients of group I and 8 patients of group II. In the other patients, irresectability was ascertained intraoperatively. All patients were subjected to preoperative pathological diagnosis either by endoscopy or FNA. There was no noticeable difference between pre- and postoperative laboratory findings of the two groups (Table 1). A significant decline in serum bilirubin, liver enzymes and jaundice was observed in all the patients postoperatively, with remarkable clinical improvement. On comparison of the operative details, the mean operative time and mean intraoperative blood loss was significantly less in group I ($P<.05$). The length of postoperative enteral feeding and duration of hospital stay was also found significantly less in group I ($P<.05$). Two patients in each group had minor postoperative complications (group I, one wound infection, one left basal atelectasis; group II, one wound infection, one minor anastomotic bile leak) that were managed conservatively. There were no cases of operative mortality or anastomotic leak in either group. The overall survival time was 8.2±3.7 months in group I and 8.1±4.1 months in group II. Two patients in group II and one patient in group I had to be readmitted due to local extension of the tumor causing recurrent jaundice. One patient in group II developed severe gastrointestinal bleeding caused by erosive gastritis and was managed conservatively. Duodenal obstruction occurred in one patient in group I, necessitating an endoscopic stenting.

DISCUSSION

Periampullary adenocarcinoma includes a diverse group of lesions around the ampulla of Vater displaying identical clinical features but associated with different prognoses. Most of such lesions are pancreatic head adenocarcinomas; 5% to 20% of them are resectable for cure at the time of appearance;[4-9] 70% of patients develop obstructive jaundice with pancreatic cancer at some point in their clinical course.[5-8] Biliary obstruction impairs liver function which can lead to hepatic failure, 25% of patients develop agonizing pruritis which cannot be relieved by medical means. Some form of palliation, therefore, becomes necessary to give respite to these patients from their agonizing symptoms and improve the quality of their life.

Patients with periampullary adenocarcinoma are mostly unresectable at the time of diagnosis. Often they need some procedure for relieving the biliary obstruction. Aided by modern radiological modalities, identification of patients with advanced disease forms a subset of patients who may be served better by endoscopic

Table 1. Main outcomes of the hepaticocholecystoduodenostomy (HCD) compared with choledochojejunostomy (CDJ).

	Group I (HCD) Mean (SD)	Group II (CDJ) Mean (SD)	*P* value
No. of cases	10	10	
Operative time, min	84.7 (10.3)	133.6 (8.9)	<.0001
Operative blood loss, mL	137.8 (37.2)	201.6 (23.4)	.0002
Onset of enteral feeding, day	3.3 (0.5)	5.0 (0.7)	<.0001
Days of hospitalization	7.5 (0.7)	9.7 (1.2)	<.0001
Serum bilirubin, μmol/L			
Preoperative	165.41 (62.71)	200.77 (69.43)	.005[a]
Postoperative	82.79 (34.42)	105.91 (49.66)	.005[b]
Serum ALP, IU/L			
Preoperative	862.2 (237.7)	998.5 (597.9)	.005[a]
Postoperative	420.8 (136.7)	4.3.6 (280.7)	.005[b]
Serum SGOT, IU/L			
Preoperative	84.2 (23.2)	74.3 (19.6)	.005[a]
Postoperative	54.2 (14.0)	45 (13.8)	.005[b]
Serum SGPT, IU/L			
Preoperative	56.0 (23.6)	52.3 (17.0)	.005[a]
Postoperative	32.0 (7.7)	33.6 (9.0)	.005[b]

Abbreviations used, ALP, alkaline phosphatase; SGOT, serum glutamic.oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase; [a]*P* value in HCD group; [b]*P* value in CDJ group.

stenting. However, a significant group of patients initially felt to have operable tumors are still found to have unresectable disease upon exploration. Additionally, there is a group of patients in whom either stenting has failed or stents get repeatedly blocked. In such a group surgical biliary bypass becomes mandatory. The aim of any operation undertaken for palliation in patients with unresectable periampullary cancer is to use the simplest procedure with the lowest incidence of immediate complications, such as anastomotic leak and recurrent biliary obstruction requiring reoperation. The accepted decompressive surgical options for treating the malignant distal biliary obstruction are cholecystoenterostomy and choledochoenterostomy.[10] A review of the literature reveals conflicting opinions on the operation of choice in such patients.[1,2] Advocates of cholecystoenterostomy claim that the operation is simple, quick and capable of relieving jaundice with minimal blood loss1 and those who side with choledochoenterostomy hold that the gallbladder and cystic duct are not dependable for biliary decompression.[2,11]

The use of gallbladder for biliary decompression in periampullary tumors creates an apprehension that the primary tumor may relentlessly creep upwards by direct extension along and around the common bile duct and obstruct it. Addressing this concern, Sarfeh et al concluded that choledochoenterostomy is significantly a more effective method of palliation than one involving the use of the gallbladder; describe it as the procedure of choice.[10] In a recent study comparing cholecystojejunostomy with choledochojejunostomy in patients with unresectable pancreatic cancer, Urbach et al concluded that there was 4.4 times increase in the risk of requiring a subsequent biliary drainage procedure in the cholecystojejunostomy group.[12] They also observed that shorter survival in CJ group was possibly related to sepsis due to inadequate biliary drainage noticed in these patients. The patency of the cystic duct, the level of its entry and relationship to the obstructing tumor seem to be the cardinal factors which determine the drainage results when the gallbladder is considered for biliary decompression. Keeping these facts in view, it is recommended that palliative biliary bypass be attempted by choledochojejunostomy rather than by cholecystojejunostomy.

Less operative time, minimal blood loss, early enteral feeding and shorter hospital stay makes the HCD procedure look attractive. While both methods effectively reduce the bilirubin levels, the development of recurrent jaundice seems to be lower after HCD possibly due to lower rate of anastomotic invasion by the tumor cells due to comparatively higher placement of the anastomosis. HCD may also offer a more physiologic operation as against Roux-en-y choledochojejunostomy, since it keeps the duodenum bathed in alkaline secretion, thereby neutralizing gastric acid and maintaining normal feedback mechanism of gastrointestinal secretions. This could result in a lower rate of ulcer formation vis-à-vis Roux-en-y choledochojejunostomy.

One patient in our CDJ study group came down with hemorrhagic gastritis requiring blood transfusion. This again looks to be healthy indicator and compares favorably with other studies where gastrointestinal bleeding following CDJ ranged between 4.7% to 15%.[13,14] It also saves extending the operating field below the mesocolon and importantly in already poorly nourished patients, it does not remove from function a segment of jejunum. A similar type of procedure described by Vankemmel et al has been performed with excellent results in patients with chronic pancreatitis.[15] In the Vankemmel procedure, after resection of the cystic duct, the neck of the gallbladder is anastomised (end to end) to the common bile duct and later the fundus of the gallbladder is anastomised to the second part of the duodenum. The difference between Vankaemmel's and our procedure is that we mobilize the neck of the gallbladder taking care not to injure the cystic artery and perform a side-to-side anastomosis rather than and end-to-end anastomosis between the common hepatic duct and the neck of the bladder. Thus, the anastomosis is placed higher and the patent cystic duct acts as an additional conduit for the passage of the obstructed bile.

Advanced periampullary adenocarcinoma patients have shorter mean survival time, as such prophylactic gastrojejunostomy seems unnecessary as most of them do not survive long enough to develop late gastric outlet obstruction and where they do, one can resort to endoscopic duodenal stenting. Minimal surgical dissection and manipulation seem to be the important factors involved in early return of bowel sounds.[16] It has been hypothesized that abdominal surgery initiates a scenario of inflammatory events that results in common clinical phenomenon of post surgical ileus.[17] Thus, surgical manipulation and the extent of dissection seem to correlate well with the return of bowel sounds. Patients who undergo HCD are subjected to minimal surgical dissection and manipulation and as such experience early return of bowel sounds leading to early return to oral feeding and hence early discharge from the hospital. These visible advantages may lure surgeons to perform HCD in patients lined for a palliative bypass. Recent studies have revealed that laparoscopic bypass, whether cholecystojejunostomy or choledochojejunostomy, is technically feasible, safe and performed within a reasonable period.[18,19] It is conceivable that, in the not too distant future, these laparoscopic techniques can be extended quite efficiently to HCD to make it more effective. Our study suggests that HCD is an effective procedure for palliative decompression in patients with advanced periampullary tumors. However, further research is needed before it can recommended as a standard procedure in such situations.

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brief report

Surgical resident satisfaction with the current surgical training program in the Riyadh area

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Ann Saudi Med 2009; 29(5): 388-392

BACKGROUND: The satisfaction of surgical residents with their training programs plays an important role in dictating its output. This survey was conducted to explore the satisfaction of surgical residents with their training programs in the Riyadh area.

METHODS: A survey questionnaire was distributed in four major hospitals to explore the view of surgical residents regarding their training programs. Frequency tables were generated for each question in the survey.

RESULTS: About 78 survey forms were distributed and 52 were retrieved (67%). About 45% of residents had a comprehensive orientation on admission to the program, but only 20% felt it was helpful. Only 40% of residents felt that their trainers were committed to training and that the consultants who were trained abroad were more committed than those trained locally (62% *vs* 36%, *P*=.01). Only 15% felt the residents themselves had enough bedside teaching or operative experience. Seventy-eight percent of the residents felt that current training does not meet their expectations. However, 85% felt that training abroad was better than local training, and 60% felt it should be mandatory. While 90% felt that training programs should be unified nationally and controlled by one organization, only 6% felt that the current governing body was capable of monitoring the training. Moreover, only 28% felt that current reviews of programs by the governing body are effective.

CONCLUSIONS: These results show that surgical residents are generally dissatisfied with current training programs. The study suggests that there are significant weaknesses in the current programs and the governing body may be ineffective in monitoring the programs. We feel that a national review of surgical training programs is warranted in view of these results.

Satisfaction of trainees with their training program is one of the most important factors affecting its output. This has been shown in other health care training fields, and found to be an indicator of quality processes.[1] Health care in Saudi Arabia enjoys wide support from many government sectors with multiple health care systems operating many hospitals with varying levels of care. Surgical training in Saudi Arabia has gone through some phases of change involving the authority charged with monitoring the training programs. While it is understood that universities are responsible for training residents in many countries, currently the Saudi Commission for Health Specialties (a government organization) oversees all aspects of training. These include program design, training center accreditation, resident selection, the course and final exams, and also physician certification and licensing. The satisfaction of Saudi surgical residents with their training programs has not been assessed. This survey was conducted to explore the satisfaction of surgical residents with their training program in the Riyadh area.

METHODS

A survey questionnaire was designed to explore the view of surgical residents regarding many aspects of their training programs, which included program orientation, mentoring, faculty role, hospital role, academic activities, clinical activities including operative experience, evaluation process, external training and training policies and monitoring. Two epidemiologists (among the authors of the manuscript) had designed the questionnaire, and a few clinicians were consulted to review and suggest any modifications. The survey contained direct questions with two responses: yes and no. We elected to design the survey with direct questions after consulting with a few professionals in the field who were interested in the subject. We also wanted to avoid any gray-zone opinions which could render the survey results equivocal. In addition, we believed that direct questions with few answer options improve response rates. The survey was distributed to all surgical residents rotating in four major hospitals in the Riyadh area between July 2007 and January 2008. These included King Faisal Specialist Hospital and Research Center, King Abdulaziz Medical City, King Khalid University Hospital, and The Armed Forces Hospital. These hospitals were chosen due to their reputable established surgical programs and the presence of a relatively high number of trainees among their staff. Concerned program directors were notified by the authors prior to survey distribution. Completed forms were then entered in an Excel spreadsheet and SPSS version 10 statistical package (SPSS, Chicago, III) was used. Descriptive data was used in form of frequency tables, which were generated for each question in the survey. An exploratory analysis was conducted to check if advanced stage of training had affected the results. Residents in the first two years of training were compared with residents in their third to fifth year of training. A chi-square test or Fisher Exact test was used to compare proportions were appropriate. A *P* value of less than .05 was considered statistically significant.

RESULTS

The survey was distributed to 78 surgical residents and 52 forms were retrieved (67%). The response rate was comparable for different participating institutions. Surgical specialties included general surgery (64%) orthopedic surgery (13%), neurosurgery (7%), urology (7%), and plastic surgery (9%). While 45% of residents had comprehensive orientation on admission to the program, only 20% believed it was complete or helpful. Forty-nine percent had an assigned mentor during training. Only 40% of residents felt that their trainers were committed to training, with consultants trained abroad more committed than those trained locally (62% *vs* 36%, *P*=.01). Eighty-eight percent thought that residents should be withdrawn from consultants who are not committed to training. The survey showed that 53% of responding residents were committed to their training, and 75% felt that other hospital staffs were not committed to training programs. Only 38% of respondents were involved in planning their academic activities, and 84% felt that it did not meet their expectations. Only 15% were satisfied with their bedside teaching or operative experience. Only 12% had the objectives of rotations emphasized at the beginning, and although they had enough evaluations (78%), 66% found them low in quality and not helpful. Seventy-eight percent responded that current training does not meet their expectations, but 59% felt it was improving. Eighty-five percent of respondents believed that training abroad was better than local training, and 60% wanted training abroad to be mandatory. Sixty percent of respondents believed that external training should be the sole training method, but 40% thought of it as complimentary to local training. Eighty-seven percent acknowledged that Saudi residents may be more committed to training externally than locally. While 90% felt that training programs should be unified nationally and controlled by one organization, only 6% believed that the current training governing body was effective in monitoring the training. Ninety percent found that there were significant differences in training among different institutions. The effectiveness of the current review of programs by the training council was questioned by 72% of respondents. The exploratory analysis showed that there were no major differences between junior and senior trainees (Table 1).

DISCUSSION

Although medicine involves extensive theoretical preparation by medical schools, postgraduate professional training has a pivotal role in preparing practicing physicians. In particular, surgical training involves an additional facet of training; operative skills. Resident satisfaction with training programs plays a major role in its maintenance. It has been repeatedly cited by surgical programs as the most important reason for not completely filling their training posts.[2] In Saudi Arabia, surgical training programs have been modified over the last few decades with changes in the monitoring agencies governing those programs. Historically, the Arab Board for Health Specialties has overseen such training for years. In the early 1990s, the Saudi Commission for Health Specialties was founded as a national organization and hence has taken over that task. In addition, there exists few other programs operating in a few training centers with mostly theoretical preparations and examinations toward fellowships awarded pending passage of certain examinations. The latter programs have no practical aspects and are not recognized by most health authorities as the sole training of surgeons. To date, this study is the first and only attempt to explore the satisfaction of Saudi surgical residents with their training. Many factors have been identified in the

Table 1. Comparison between junior (group I) and senior (group II) residents.

Question	Total (*n*=52)	Group I (*n*=31)	Group II (*n*=21)	*P* value
Was the orientation helpful to shape your training? Yes	20%	19%	27%	0.72
Do you have a constant mentor? Yes	49%	78%	26%	0.02*
Do you believe that consultants are committed to training? Yes	40%	53%	21%	0.04*
Are you involved in planning your academic activities? Yes	38%	47%	25%	0.15
Does local training meet your expectations? Yes	22%	30%	10%	0.16
Were training objectives emphasized to you at the beginning of the program? Yes	12%	14%	10%	1.00
Do you believe that external training is better than local training? Yes	85%	86%	81%	0.69
Do you believe that external training should be mandatory? Yes	60%	66%	53%	0.53
Do you believe that external programs are more committed to training than local ones? Yes	66%	55%	82%	0.11
Do you believe that current training council is effective in monitoring training? Yes	6%	10%	0%	0.27
Do you believe that current reviews by training council are effective in improving programs	28%	40%	10%	0.26

Group I: 1st and 2nd year residents, Group II: 3rd, 4th, and 5th year residents, *: significant

literature that affect resident satisfaction with training programs. Among them are a balance between education and service,[3] the quality of attendant's teaching,[4] interaction with attendants during patient care,[4] operative experience,[2,4,5] and substantial citing of evidence-based literature.[2]

This survey showed that 78% of Saudi surgical trainees were not satisfied with current programs in response to a direct question. This was affirmed by their responses to questions regarding some of the factors shown in the literature to affect residents satisfaction with training programs. Sixty percentage of residents were not satisfied with the faculty's commitment to training, with externally-trained faculties being more committed than locally trained faculties. The latter reflects differences in the attitudes of the trainers shaped by their background training. Faculty motivation to educate residents plays an important role in the dynamics of training programs. It has been shown that there are significant differences among attending faculty members regarding education abilities[6] and that many trainers' self-assessment differed significantly from that of the residents. In general, trainees believe that they are not getting enough education by faculties.[3] It was also shown that feedback from trainees could improve the performance of trainers to a significant extent.[7] On the other hand, many factors have been shown to affect trainers' performance. Among them, time designation for education,[8] job satisfaction,[8] motivation for learning,[9,10] recognition and rewards.[11] From the above, it is obvious that the commitment of faculty members for training and the perception of trainees of such commitment is a complex process and that targeting the above factors to enhance trainers' abilities to educate trainees is essential. In fact, some suggested a comprehensive approach to faculty development,[12] and its implementation was shown to positively affect the training process.[13]

Operative experience has been shown repeatedly to be one of the most important predictors of satisfaction with surgical training.[2,4,5] Our study showed that 85% of surgical trainees were not satisfied with their operative experience. This raises major concerns regarding the quality of current training program. A unique attempt was made to evaluate the operative colorectal surgical experience of advanced general surgical residents at a tertiary care center in Riyadh.[14] In this study, the surgical experience of Saudi residents was compared with that of surgical residents at a hospital in New Zealand. It was concluded that Saudi general surgical residents were not getting enough colorectal surgical experience despite the fact that the Saudi Board criteria were likely to be met. This study was limited by the fact that it was concerned with only colorectal surgical experience during general surgical training and its results do not reflect the general operative experience in the program. Moreover, the tertiary nature of the Saudi institution with highly advanced cases, and lack of emergency procedures may have skewed the data and led to such a conclusion. Finally, we believe that such a comparison has to be made with multiple training programs with different training methods in order to draw meaningful conclusions. The author used a general term as Western type cases to indicate the type of training needed for residents, but did not discuss the nature of the programs. Western training varies from one country to the other (e.g. North American training differs from European training), but is collectively called Western training. The trainee's attitude and behavior have a major impact on operative experience,[15] and some felt that residents should "earn" operative experience as a reward for good patient care in the ward.[14]

Operative experience has to be a major component of our programs and new methodologies have to be devised and implemented to overcome current barriers. Possible barriers are trainees' attitude and behavior, faculty commitment, and the availability of a wide spectrum of cases per institution. Some have suggested the use of simulators to practice surgical procedures and adopting an apprenticeship-type model with fewer numbers of faculties per service.[2]

Recently, many medical schools have been founded in Saudi Arabia to produce enough physicians to cover local demands. Currently, only 19.3% of medical doctors are Saudis.[16] Most of the respondents prefer to be trained at centers abroad and support the notion of making external training mandatory. Training positions locally does not meet the increasing numbers of graduating medical doctors, and moreover, available external training posts are decreasing (personal communication). These facts indicate the need for expedited program reviews and expansion to accommodate the increased numbers of trainees and ensure quality of programs. Moreover, uniformity of training at different institutions is customary to enhance trainees' satisfaction with training.

About 94% of participants believe that the Saudi Council of Health Specialties (national training organization) does not ensure adequate monitoring of the training. This reflects a wide gap between the residents and their training mentors and questions the current communication channels between the two sides. We believe that a transparent relationship coupled by a real wide partnership between the Saudi Council and trainees should be established. Surgical residents deserve a fair representation at the surgical section at the Saudi Council with open channels of communication. This could provide a feedback mechanism that safeguards training and ensures its quality.

In our study, there were no major differences between junior and senior residents regarding responses except in two questions (Table 1). Most junior residents had constant mentors and believed that consultants are committed to training. It seems that this belief changes as trainees advance in the program. The fact that junior and senior residents were not different in responses reflects a general consensus on the results and adds to the validity of the conclusions. Although the exploratory analysis added some comparative data, we acknowledge that the sample size may not convey enough power for this kind of comparison, and thus its results have to be viewed with caution.

This study has a few limitations. The response rate was 67% and one may speculate that nonrespondents may differ from respondents, and thus the results of the study may not be valid. We believe that this response rate is reasonable given the nature of the study and the comparable response rate among institutions. Most of the residents who participated were general surgery trainees (64%). This reflects the fact that most of the surgical residents in training at institutions belong to general surgical programs. Moreover, the questionnaire contained general questions applicable to all surgical disciplines, and it is unlikely that the disciplines have any effect on the results. Our study was conducted in four training centers only, but since these centers are among the largest programs in Riyadh, we feel it is a true representative sample for the rest of the programs.

In conclusion, this data show a general dissatisfaction of surgical residents with their current training programs. It also suggests significant weaknesses of the current program and the ineffectivity of the current monitoring mechanism. We feel that a national review of surgical training programs is warranted in view of these results. These data should be used as a baseline to monitor the effectiveness of interventions applied in the future toward improving surgical training programs.

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An unusual cause of gastric outlet obstruction: a pancreaticoduodenal artery aneurysm

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Ann Saudi Med 2009; 29(5): 393-396

We present a rare case of gastric outlet obstruction due to compression of the duodenum by a pancreaticoduodenal artery (PDA) aneurysm 2.5 cm in diameter, in a 43-year-old man from Saudi Arabia who presented with persistent vomiting and epigastric pain. The initial investigations and blood works were negative, and esophagogastroduodenoscopy (EGD) was unremarkable. A CT abdomen demonstrated a mass around the duodenum and dilatation of the stomach, and CT angiography showed the PDA aneurysm. The patient was stabilized and then referred to a tertiary center for embolization. Our case demonstrates a diagnostic challenge that physicians may encounter in patients who present with vomiting and epigastric pain.

Pancreaticoduodenal artery (PDA) aneurysm is a rare type of visceral artery aneurysm, which also includes splenic, renal, hepatic, mesenteric, and aortic arteries aneurysms.[1] PDA aneurysms have nonspecific clinical presentations,[2] which explains why they are not usually considered in the differential diagnosis of patients who present with epigastric pain or vomiting. We report a case of a patient with a PDA aneurysm who presented with repeated vomiting and epigastric discomfort. The aneurysm was found incidentally in a CT scan of the abdomen. Visceral angiography was done to visualize the aneurysm and the diagnosis of PDA aneurysm causing a gastric outlet obstruction was confirmed. The patient was referred to a specialized center and was successfully treated.

Although the PDA aneurysm was reported in many cases, the presentation as gastric outlet obstruction is rare. Commonly, gastric outlet obstruction is caused by gastric and peripancreatic malignancies in developed and developing countries.[3] Peptic ulcer disease is the most common benign cause of gastric outlet obstruction.[4] We present this case to draw attention to the fact that PDA and other visceral aneurysms are rare causes of gastric outlet obstruction, which should be considered if none of the more common causes of gastric outlet obstruction can be identified.

CASE

A 48-year-old Saudi man presented with repeated vomiting and epigastric discomfort for a duration of ten days. Vomiting occurred one hour after eating, and was projectile, yellowish in color, and contained undigested food with no mucus or blood. It was associated with mild epigastric discomfort, which was of gradual onset, intermittent, dull and aching in nature, and occasionally felt in the back and both hypochondria. There was no history of peptic ulcer disease or drug ingestion. The patient denied any history of fever, cough, weight loss, or trauma. He was diagnosed with hypertension 10 months before presentation for which he was taking fosinopril 10 mg once daily. The family history was negative for aneurysms and malignancies. The patient was retired from the military services. He drank alcohol occasionally and had a 10 pack-year smoking history.

Clinical examination revealed a middle-aged man who was fully conscious, afebrile, and hemodynamically stable. Systemic examination revealed no abnormality, but abdominal examination revealed mild tenderness in the epigastric area. The rectal examination was unremarkable. Blood tests were unremarkable (Table 1) Esophagogastroduodenoscopy revealed hiatus hernia with mild gastritis not consistent with the clinical condition of the patient. A gastric biopsy was negative for malignancy. A CT scan of the abdomen demonstrated a rounded structure in the posterior aspect of the pancreas, anterior to the third part of duodenum, which measured 2.5 cm and compressed the duodenum, causing dilatation in the stomach, and the first and second part of the duodenum, which suggested an aneurysm in PDA or gastroduodenal (hepatic) artery (Figure 1). A CT angiography suggested by the radiologist confirmed the diagnosis of PDA aneurysm causing gastric outlet obstruction (Figure 2). The patient received supportive treatment and was referred to a tertiary center for embolization of the aneurysm.

Table 1. Laboratory investigations.

Complete blood count and coagulation profile

White blood cell count: 17.8×10^3 cells per mm^3

Hemoglobin: 11.7 g/dL

Hematocrit: 35.2%

Platelets: 585 000 per mm^3

Mean corpuscular volume: 65.8 fL

Mean corpuscular hemoglobin: 21.9 pg

Prothrombin time: 14.6 seconds

International normalized ratio: 1.09

Partial thromboplastin time: 34.4 seconds

Renal profile

Sodium: 142 meq/L

Potassium: 3.7 meq/L

Chloride: 100 meq/L

Bicarbonate: 27 meq/L

Urea: 6.8 mmol/L

Creatinine: 89 μmol/L

Glucose: 7.2 mmol/L

Anion gap: 15

Liver function tests

Lactate dehydrogenase: 404 U/L

Alanine aminotransferase: 107 U/L

Alkaline phosphatase: 163 U/L

Albumin: 44 g/L

Total protein: 80 g/L (60-85 g/L)

Amylase: 77 U/L

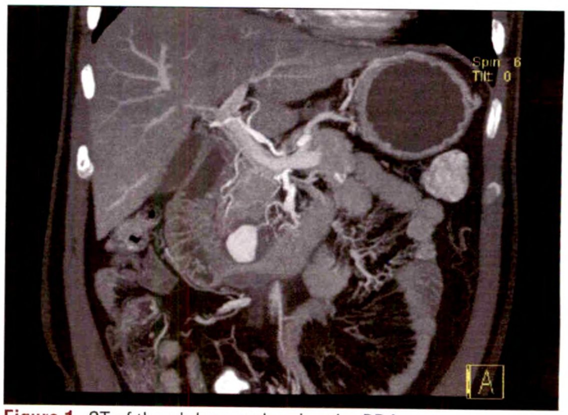

Figure 1. CT of the abdomen showing the PDA aneurysm.

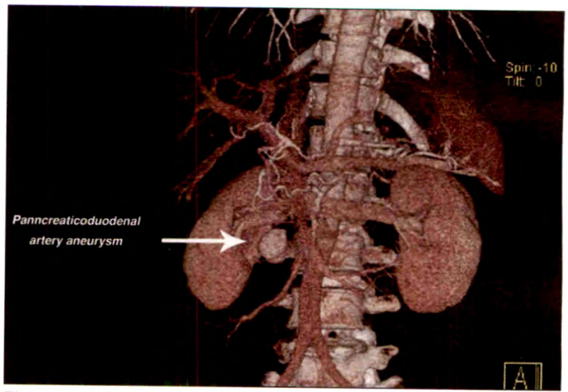

Figure 2. CT angiography slowing the pancreaticoduodenal artery aneurysm.

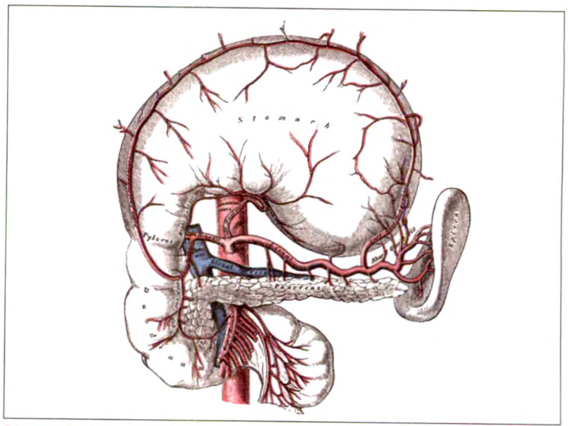

Figure 3. The superior and inferior PDA arteries pass close to the duodenum and gastric outlet.

DISCUSSION

PDA aneurysms are very rare. They comprise 2% of all visceral artery aneurysms.[5] Since Ferguson et al reported the first case of PDA aneurysm in 1895,[6] 88 cases of PDA aneurysms were reported in the English literature until 1993 and 52 cases of PDA aneurysms were reported between 1973 and 1999.[7] More reported cases increased awareness as to the importance of early detection before rupture.

Men are four times as likely as women to have PDA aneurysms.[8] The vast majority of patients with these aneurysms experience epigastric pain and discomfort. This may be secondary to underlying pancreatic disease in 30% of PDA aneurysms.[8] Other clinical presentations include hemosuccus pancreaticus–which is the presence of bleeding into the pancreatic duct–or hemobilia, jaundice, and shock.[9]

Reported cases of PDA aneurysms have also included a case that presented with vaginal bleeding and incidentally was found to have a pulsatile mass on ultrasound examination.[10] Another case presented with an incarcerated inguinal hernia that subsequently hemorrhaged into the retroperitoneum from a ruptured PDA aneurysm.[10] Itoh et al reported a case of PDA aneurysm causing pancreatic pseudotumor and duodenal obstruction, which on angiography was an aneurysm of 8 mm in diameter, found in the posterior superior PDA.[11] Androulakakis et al reported a case of a gastric outlet obstruction caused by giant gastroduodenal artery aneurysm.[12] Chiou et al reported a case of pancreaticoduodenal artery aneurysm that began with intestinal angina and weight loss.[13]

The most common cause of these aneurysms is pancreatitis-related vascular necrosis or vessel erosion by an adjacent pancreatic pseudocyst.[8] Othe causes also include atherosclerosis, infection, congenital defects, fibromuscular dysplasia, connective tissue disorders (polyarteritis nodosa or Takayasu arteritis) and trauma.[1,8] Our patient had atherosclerosis risk factors which included a past history of hypertension and a 10-pack year smoking history. Alcohol consumption is also a risk factor for pancreatitis; Any of these factors might have been the cause of his aneurysm.

Gastric outlet obstruction is commonly caused by gastric malignancy or stenosis of the pylorus as a complication of chronic peptic ulceration.[14] Other benign differential diagnoses of gastric outlet obstruction include infections such as tuberculosis and infiltrative diseases such as amyloidosis. Gastric outlet obstruction may also be caused by gallstone, a condition termed as Bouveret syndrome. Superior and inferior PDAs communicate anteriorly to the head of the pancreas and medial to the first part of the duodenum (Figure 3).[15] Arteriography is necessary to confirm the existence of PDA aneurysms. CT or magnetic resonance angiography (MRA) are also of importance in recognizing these aneurysms and are helpful in detecting the presence of rupture or associated pancreatic disease.[10] In our case, a contrast-enhanced CT scan of the abdomen revealed the aneurysm from the PDA, which has a blood supply from both the superior mesenteric artery and gastroduodenal artery and measures 2.5 cm, causing narrowing of the transverse duodenum with dilatation of stomach, and the first and second part of the duodenum.

We believe that PDA aneurysms and other visceral aneurysms should be considered in any patient who presents with repeated vomiting and gastric outlet obstruction symptoms, especially if no cause can be found.

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case report

Strongyloides stercoralis hyperinfection after corticosteroid therapy: a report of two cases

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Ann Saudi Med 2009; 29(5): 397-401

Two cases of *Strongyloides stercoralis* hyperinfection are described. Both patients were expatriates from the Indian subcontinent, and reported the use of corticosteroids. The first patient presented with severe pulmonary disease that necessitated respiratory support, followed by acute abdomen and intestinal obstruction and he succumbed to these diseases. The second patient also presented with acute pulmonary disease, which responded to antihelmintic treatment and supportive care; however, he died later due to his primary disease. The clinical features of *S stercoralis* hyperinfection are nonspecific; therefore, a high index of suspicion is required for early diagnosis and to start appropriate therapy. Because of the seriousness of the disease and the associated high mortality we suggest screening for *S stercoralis* in patients from endemic areas who will be taking immunosuppressive therapy.

Strongyloides stercoralis is a ubiquitous soil transmitted intestinal nematode of humans that is endemic in many areas throughout the tropical and temperate regions.[1,2] The term hyperinfection is used to denote autoinfection, a phenomenon in which the number of worms increases tremendously. Development or exacerbation of gastrointestinal and pulmonary symptoms is seen, and the detection of increased numbers of larvae in stool and or sputum is the hallmark of hyperinfection. *S stercoralis* hyperinfection syndrome, well recognized since 1966, has increased in frequency during the past decades as a result of immunosuppressive therapy used in the treatment of organ transplant recipients, collagen vascular diseases and cancer.[3] Of all the immunosuppressive drugs, corticosteroids are the most widely used and the most specifically associated with transforming chronic strongyloidiasis to hyperinfection.[4] The outcome in patients with hyperinfection remains poor with 50% mortality despite therapy.[5] We report two cases of *S stercoralis* hyperinfection following corticosteroid therapy with fatal outcome.

CASE 1

A 44-year-old Bangladeshi male was admitted to Hamad General Hospital on 31 December 2004 with progressive shortness of breath, fever, and productive cough with yellowish sputum of four days duration. His past history was remarkable for chronic obstructive pulmonary disease (COPD), secondary polycythemia, pulmonary hypertension, and old pulmonary tuberculosis. He was maintained on salbutamol inhaler, fluticasone, and salmetrol discus inhaler, theophylline and home oxygen therapy. He denied receiving systemic corticosteroids in the preceding year. He was an ex-smoker and alcohol drinker. Physical examination on admission revealed an ill looking, dyspneic patient with a temperature 38.4°C, blood pressure 135/90 mm Hg, pulse rate 160/minute, and respiratory rate 36/minute. Chest examination revealed expiratory wheezes and bilateral basal crepitations. Otherwise, physical examination was unremarkable. Laboratory investigations revealed hemoglobin 13 mg/dL, white blood cell count (WBC) 14.6×10^9/L (neutrophils 82%, lymphocytes 10%), platelets 25×10^9/L, glucose 11.4 mmol/L, creatinine 135 mmol/L, sodium 129 mmol/L, potassium 3.8 mmol/L. Arterial blood gases revealed pH 7.19, PCO_2 74.8 mm Hg, PO_2 96 mm Hg. Chest radiograph showed no lung infiltrates. Sputum culture grew *Pseudomonas aeruginosa*, sensitive to ce-

fipime and ciprofloxacin; however, it was thought to represent colonization. A diagnosis of COPD with acute exacerbation was made, for which he was given intravenous ceftriaxone 2 gm once daily, azithromycin 500 mg once daily, methylprednisolone 40 mg three times daily, and salbutamol and ipratropium bromide nebulizers. He made a gradual improvement, and after seven days he was shifted to oral prednisolone 40 mg once daily and oral amoxicillin/clavulanic acid to complete two weeks of antibiotics. Prednisolone was given for a total of 13 days. Three weeks after admission he developed hemoptysis, chest tightness, and worsening cough. Sputum culture grew *P aeruginosa* for which he was given intravenous cefepime and ciprofloxacin. Sputum smear for acid fast bacilli (AFB) was negative. Because of worsening respiratory status and a chest radiograph showing an infiltrate involving the whole left lung and part of the right lung, bronchoscopy was performed on 27 January 2005. No endobronchial lesion was found. Antituberculous drugs in the form of isoniazid, rifampin, pyrazinamide, and ethambutol were started. Bronchioalveolar lavage and bronchial wash were negative for AFB but bacterial culture grew *P aeruginosa, Escherichia coli, and Klebisella pneumoniae*. Cytologic examination of the bronchial wash and lavage revealed bronchial epithelial cells, few squamous cells in the background of numerous *S stercoralis* worms (Figure 1) and bacteria with inflammatory cells and blood. Transbronchial biopsy showed only intraalveolar hemorrhage with anthracotic pigments, but was negative for granuloma, viral inclusions, or malignancy. He was treated with oral ivermectin 12mg once daily. Two days later he complained of vomiting, lower abdominal pain, abdominal distention, and constipation. Physical examination revealed abdominal distention, lower abdominal tenderness, and sluggish bowel sounds. A plain radiograph of the abdomen revealed distended bowel loops but no air fluid levels. Lapratomy was done. The findings at surgery were a dilated jejunum and ileum filled with stool. Microscopic examination of the resected part of the ileum bowel revealed acute inflammation, mucosal hemorrhage, and focal ulceration with abundant *S stercoralis* larvae (Figures 2 and 3). Postoperatively, he was mechanically ventilated. His postoperative course was complicated by hypotension and multiorgan failure and he expired after two days.

CASE 2

A 39-year-old Nepali male was diagnosed with multiple myeloma complicated by spinal cord compression on

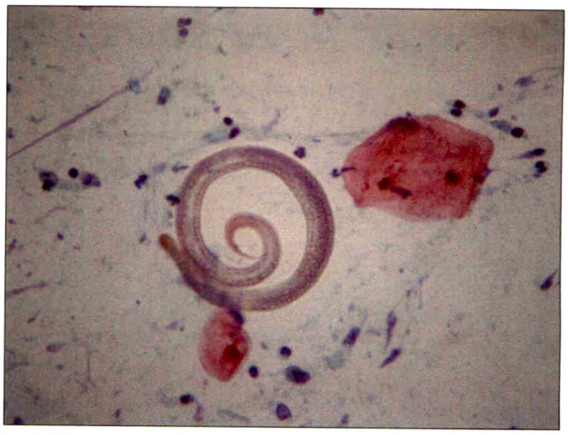

Figure 1. Cytologic examination of the bronchial wash showing a *S stercoralis* worm in a background containing some cellular debris (Papanicolaou stain ×400).

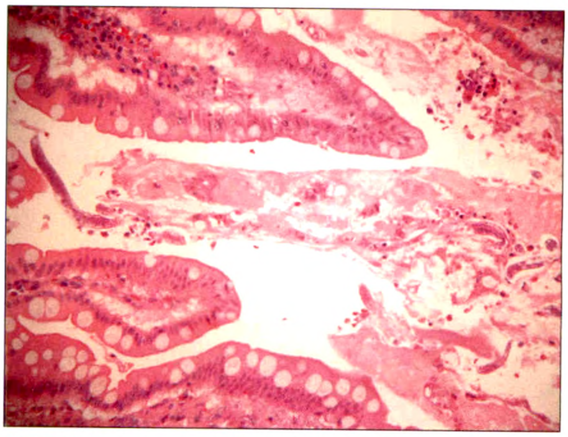

Figure 2. Low power view of the resected small bowel showing numerous larvae of *S stercoralis* in the mucinous material in between the villi (hematoxylin and eosin ×100).

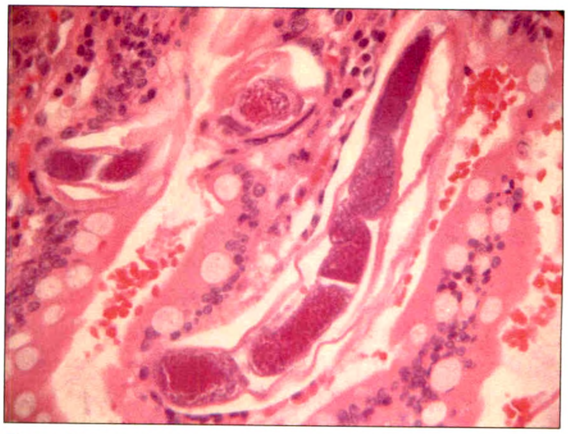

Figure 3. High power microscopic view showing larvae embedded within the small bowel villi. Notice the dark purplish organs surrounded by translucent sheath (coat) (hematoxylin and eosin ×400).

17 June 2007, for which he received radiotherapy and dexamethasone which was given for a total of six weeks. On 4 July 2007, he developed shortness of breath and hemoptysis associated with purpuric skin rash so he was transferred to intensive care unit. His past history was unremarkable. Physical examination revealed temperature 38°C, blood pressure 90/60 mm Hg, pulse rate 120/minute and respiratory rate 22/minute. Chest examination revealed bilateral fine crepitations up to the middle zone. Examination of the skin revealed palpable purpuric skin rash with vesicles involving the trunk and both upper thighs.

Laboratory investigations revealed hemoglobin 8.3 mg/dl, WBC 7.3×10^9/L (eosinophils 4.2%, lymphocyte 2.2%, neutrophil 92.1%), platelets 68×10^9/L, ESR creatine and electrolyte levels 81 mm/hr, ALT 109 U/L, AST 59 U/L, albumin 24 g/L, total protein 45 g/L. He had normal renal function tests. Arterial blood gases revealed pH 7.463, $P\text{CO}_2$ 32 mm Hg, $P\text{O}_2$ 63.6 mm Hg, and oxygen saturation of 93.3% on room air. Chest radiography showed diffuse bilateral reticular nodular and patchy infiltrate with multiple osteolytic lesions involving the lateral aspect of the right ribs (6th, 7th, and 8th ribs). Sputum examination revealed larva of *S stercoralis* and culture grew *K pneumoniae*. Blood and urine cultures were negative. His condition deteriorated rapidly, so he was mechanically ventilated. He was treated with intravenous pipercillin-tazobactm 4.5 gm 8 hourly, ciprofloxacin 400 mg 12 hourly. A diagnosis of strongyloides hyperinfection syndrome was made, for which he was given intravenous albendazole 400 mg once daily for two days then oral ivermectin 9 mg once daily. Three stool samples for *Strongyloides* were negative. Repeated sputum examination for *S stercoralis* was positive until 4 August after which ivermectin was discontinued. Skin biopsy showed evidence of herpes zoster with leukocytoclastic vasculitis with no evidence of cutaneous strongyloidiasis. Acyclovir 700 mg 8 hourly was added to his treatment regimen after receiving the biopsy result. Several days later he developed acute generalized motor neuropathy for which he underwent tracheostomy anticipating the long stay on ventilator. The cause of neuropathy was thought to be critical illness neuropathy.

On 5 August 2007, he developed fever, and neck stiffness. Lumber puncture revealed xanthochromic fluid. Cerebrospinal fluid (CSF) examination revealed WBC 130 cells/mL (neutrophils 25%, lymphocytes 80%), protein 3.57 mg/L, and glucose 4 mmol/L. The CSF was negative for India ink, bacterial latex antigen, AFB, or *S stercoralis* larvae with negative bacterial culture. He was started empirically on intravenous ampicillin 2 gm every 4 hours, cefepime 2 gm every 8 hours for possible meningitis, and ivermectin was restarted. Later on blood and CSF cultures came to be negative; however, urine and endotracheal cultures grew *P aeruginosa*. One day after starting antibiotics, the fever subsided and the patient became conscious. On 15 August the patient was found unconscious with fixed dilated pupils. CT head revealed extensive intraventricular hemorrhage with slight dilatation of all the ventricles and he expired one day later. The cause of intracerebral hemorrhage could not be ascertained since he had normal platelets, prothrombin, and activated partial thrombin times at the time of neurologic deterioration.

DISCUSSION

Infection with *S stercoralis* was first reported in the year 1876 in French soldiers on duty in Vietnam.[2] The first report of disseminated infection or hyperinfection dates back to 1966, when Cruz et al and Rogers et al. independently documented the occurrence of fatal strongyloidiasis with immunosuppression.[3,6] The term hyperinfection is often used to denote autoinfection, a phenomenon in which the number of worms increases tremendously and worms are detectable in extraintestinal sites, especially the lung.[2] Patients with impaired cellular immunity, especially those receiving long-term steroids, HTLV-1 and HIV-infected patients, and those with hematologic malignancies, transplant recipients, are at risk of developing the hyperinfection syndrome.[2-4] Most of the patients who develop hyperinfection syndrome are receiving corticosteroids often for COPD. Pulmonary strongyloidiasis may mimic COPD exacerbation.[2,7,8] Hyperinfection may develop as early as 20 days after the onset of corticosteroid therapy[9] and as late as several years.[10]

The manifestations are a combination of gastrointestinal, pulmonary, and constitutional symptoms. The intestinal manifestations include severe cramping, abdominal pain, watery diarrhea, weight loss, nausea, vomiting, and occasionally gastrointestinal bleeding and small bowel obstruction.[4] Pulmonary manifestations include mainly asthma-like symptoms such as cough and wheezing, and others such as pneumonia, pulmonary hemorrhage, pleural effusion, and acute respiratory failure.[4,5] Hyperinfection may be complicated by bacterial infections and bacteremia caused by gut flora.[4,11] Definitive diagnosis of strongyloidiasis is usually made on the basis of detection of larvae in stool or sputum.[2,12] However, relying on stool studies alone for screening is inadequate. A single stool exam is said to be approximately 50% sensitive for making the diagnosis.[2] The blood agar plate culture method, in which the serpiginous tracks of bacterial growth along the paths of motile larvae become apparent after 1 or 2 days of incubation at room temperature, is a preferred method because of its high sensitivity and ease of implementation in standard microbiology laboratories.[2,13] Methods to sample duodenal fluid are more invasive and therefore less desirable. Serologic testing is now widely available and is sensitive but not specific.[2] A single test does not reliably distinguish past from current infection.[2,14] Albendazole, mebendazole, thiabendazole, and ivermectin have been shown to be effective for *S stercoralis* infection.[15,16] Recently, there has been a change in the treatment of strongyloidiasis with more studies showing ivermectin as the drug of choice.[17] Monitoring the response to treatment could be very difficult with detection of strongyloid larvae in the stool specimen because of the inconsistent shedding of the larvae.[18]

S stercoralis hyperinfection is rare in our area. Medline search from 1966 revealed only one report from Kuwait.[19] In addition to the current two patients, we are aware of only one more case that was reported from Qatar in 1992.[20] All three patients were from the Indian subcontinent, suggesting that *S stercoralis* hyperinfection in Qatar is a disease of the expatriate population especially those originating from the Indian Subcontinent.

The presentation in our patients was similar in many aspects to that described by others. Both patients presented initially with severe pulmonary disease that necessitated mechanical ventilation. These clinical features are nonspecific, therefore a high index of suspicion is needed for early diagnosis. Although, the mortality in patients with *S stercoralis* hyperinfection has been reported to be 50%, the fatal outcome in both of our patients is of concern and indicates the need for increasing awareness among physicians of this curable but potentially fatal disease. It is of interest that the first patient developed the hyperinfection syndrome after receiving a short course of corticosteroid therapy (13 days only). Both the fatal outcome in our patients and the development of the condition after a short course of corticosteroid therapy suggests the need to be vigilant in such patients to allow for early diagnosis and institution of appropriate treatment in order to avoid such unfortunate outcome. *S stercoralis* can remain quiescent in the host's intestine for as long as 30 years,[5,21] becoming apparent when the host immunity decreases as a result of immunosuppressive drugs and/or disease. Physicians in the Gulf area should be aware of this. Although it is hard to draw conclusions from two cases, it may not be unreasonable to screen immunocompromised patients from endemic areas by serology before initiating steroid therapy to prevent the development of *Strongyloides* hyperinfection. Screening is not recommended for patients before starting short courses of corticosteroids for bronchial asthma or COPD, but may be considered in severe cases of bronchial asthma or COPD requiring recurrent and frequent steroids courses.

In conclusion, *S stercoralis* hyperinfection syndrome is a disease of immunocompromized patients, especially those who are receiving systemic steroids. Early diagnosis is a real challenge. Clinicians should be aware of the possibility of hyperinfection in immunocompromized patients, and that it may mimic other diseases leading to misdiagnosis.

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Ileosigmoid knot: a case report and literature review of 280 cases

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Ann Saudi Med 2009;29(5): 402-406

Ileosigmoid knotting, also known as compound volvulus or double volvulus, is a rare cause of intestinal obstruction. In this condition the ileum wraps around the base of the sigmoid colon and forms a knot. Ileosigmoid knotting is an unusual entity in the West, but is comparatively common in certain African, Asian and Middle Eastern nations. The condition is serious, generally progressing rapidly to gangrene. Awareness of the condition is essential for prompt diagnosis and optimal management. This report describes a case in a 60-year-old male and describes the management of this rare condition. An additional 280 recent cases in the English literature are reviewed as to etiopathogenesis, presentation, diagnostic modalities, surgical interventions and outcome.

Ileosigmoid knotting (ISK) is a rare cause of intestinal obstruction that rapidly progresses to gangrene of the ileum as well as the sigmoid colon.[1] Preoperative diagnosis is difficult because of its infrequency and atypical radiographic findings.[2,3] It is essential to differentiate it from sigmoid volvulus because endoscopic reduction is a contraindication in ISK. In recent years, CT has been helpful in making a preoperative diagnosis. Generalized peritonitis and sepsis is the main cause of poor outcome.[3,4] After hemodynamic stabilization, immediate surgical intervention is the need of the hour.

CASE

A 60-year-old male patient with a history of chronic constipation was admitted with severe lower abdominal pain of 24-hour duration. This was associated with progressive abdominal distension and vomiting. He was in distress and was dehydrated. Examination revealed a BP of 100/60 mm Hg, pulse rate of 98/min, and temperature of 38.5° C. Abdominal examination revealed diffuse abdominal distension, tenderness, and guarding. Laboratory data showed a white cell count of 20 000/mm^3, hemoglobin level of 9.6 gm%, C-reactive protein of 12.7 mg/dL (normal range, <0.3 mg/dL). Plain film of the abdomen showed dilatation of the small intestine with a gas and air fluid level, with an associated moderately distended, and obstructed sigmoid loop. A CT scan was planned, but could not be carried out for technical reasons. The patient was resuscitated with IV fluids and started on IV cefuroxime and metronidazole and was taken up for laparotomy 4 hours after admission for suspected ISK based on both the small gut and sigmoid colon obstructive features on plain x-ray of the abdomen. On laparotomy, hemorrhagic fluid was encountered and the ileum and sigmoid colon was found to be gangrenous with a 360° clockwise twist of the ileum around the sigmoid colon. In addition, a Meckel diverticulum with a small band was found at the base of the twist (Figure 1). Following a 100-cm resection of

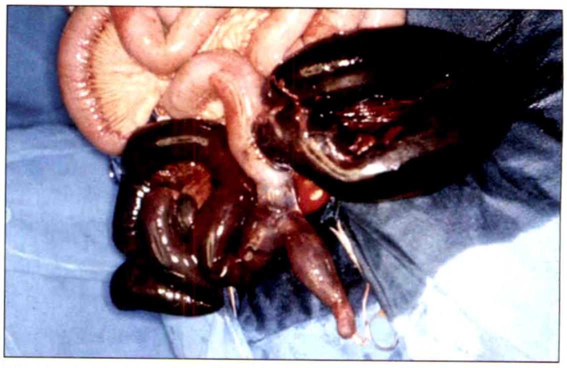

Figure 1. Ileosigmoid knot with gangrenous ileum and sigmoid colon and Meckel's diverticulum.

Table 1. Demographics and clinical features.

Author (year)	No. of cases	Age mean/ range	Sex M:F	Duration of symptoms in hours mean/range	Symptoms P	D	V	C	M	S	Pre-diagnosis
Bawa, 2008	1	26	1:0	>240	1	1	1	1	-	-	0
Atamanalp, 2006	9	10.6 7-16	7:2	24-72 45.3	9	9	9	9	3	3	0
Berrebi, 2006	1	9	0:1	12	1	1	1	-	-	1	0
Hirano, 2005	1	75	1:0	28	1	1	1	-	-	-	1
Atamanalp, 2004	63	47 7-75	47:16	12-120 46.6	63	60	53	63	9	38	0
Hashimato, 2004	2	32 4-60	2:0	26	1	2	-	-	1	-	1
Tamura, 2004	1	78	1:0	?	1	1	-	-	-	-	1
Raveenthiran, 2001	7	43 30-60	6:1	6-240 (53)	7	6	5	7	-	4	5
Akgun, 1997	16	45 20-90	11:5	1-144 (100)	16	15	14	-	-	9	?
Alver, 1993	68	49 18-79	57:11	24-144 (33)	68	64	59	64	-	38	0
Miller, 1992	1	41	0:1	2	1	0	1	-	-	0	0
Puthu, 1991	7	40	4:3	8-72 (36)	7	7	7	-	-	2	2
Kakar, 1981	11	38	10:1	?	11	3	11	?	?	4	2
Shephard, 1967	92	42 11-75	78:14	6-76 (18)	92	90	?	?	?	?	?

P-Pain; D-Distension; V-Vomiting; C-Constipation; M-Malaena; S-Shock

gangrenous ileum and sigmoid colon, a primary anastomosis of the small gut and colon was carried out. Except for a minor wound infection patient made an uneventful recovery and was discharged after 10 days.

DISCUSSION

Parker is credited with having described the first patient with ISK in 1845.[1] The first patient from the Asian subcontinent was reported by Paul in 1940, an account of which was given by Shepherd.[2] Since then over 280 cases have been reported in the English literature.[2-9] Three factors are responsible for the ileosigmoid knot: a long small bowel mesentery and freely mobile small bowel; a long sigmoid colon on a narrow pedicle; and finally the ingestion of a high bulk diet in the presence of an empty small bowel.[2-8] When a semi-liquid bulky meal progresses into the proximal jejunum it increases the mobility of the intestine and the heavier segments of the proximal jejunum fall into the left lower quadrant. The empty loops of ileum and distal jejunum twist in a clockwise rotation around the base of a narrow sigmoid colon. Further peristalsis forms an ileosigmoid knot with two closed loop obstruction, one in the small bowel and other in the sigmoid colon.[2-6] Evidence for the mechanism is suggested by studies carried out on Bagandans in Uganda who eat once a day and Muslims who eat a single daily meal during the Ramzan fast.[2,4] ISK is predominately seen in males (80.2%) with a mean age of 40 years (range, 4-90 years) (Table 1). Besides the above anatomic prerequisites, the literature reveals the evidence of other secondary causative factors including late pregnancy, transmesenteric herniation, Meckel diverticulitis with a band, ileocecal intussusceptions, and floating cecum (Table 2).[3,4,7,8] Among the 280 patients reviewed, 4.3% were children under the age of 16 years.[9-11] While ISK is predominately reported in certain African, Asian, and Middle-East nations, it is a rare occurrence in the white population.[10]

ISK has been categorized into three types. In type I, the ileum (active component) wraps itself around the sigmoid colon (passive component) in a clockwise or anticlockwise direction (type A when clockwise and type B when anticlockwise). In type II, the sigmoid colon (active component) wraps itself around a loop of ile-

Table 2. Secondary predisposing factors and investigations.

Author	No.	Predisposing factors						Investigations	
		LP	PS/Ad	MD	FC	IH	NS	X-ray	CT
Bawa, 2008	1	-	-	-	-	-	1	1	0
Atamanalp, 2006	9	-	-	-	-	-	9	9	0
Berrebi, 2006	1	-	-	-	-	-	1	1	1
Hirano, 2005	1	-	-	-	-	-	1	1	1
Atamanalp, 2004	63	2	10	-	1	-	-	41	0
Hashimato et al, 2004	2	-	-	-	-	-	2	2	2
Tamura et al, 2004	1	-	1	-	-	-	-	1	1
Raveenthiran, 2001	7	-	-	-	-	-	7	7	-
Akgun, 1997	16	-	-	-	-	-	16	16	-
Alver, 1993	68	4	12	1	1	4	-	56	-
Miller, 1992	1	-	1	-	-	-	-	1	-
Puthu, 1991	7	-	-	1	-	-	-	7	-
Kakar, 1981	11	-	-	-	-	-	-	8	-
Shephard, 1967	92	-	-	-	-	-	92	NS	-

LP-late pregnancy; PS-previous surgery; Ad-adhesions; MD-Meckel's diverticulum; FC-floating caecum; IH-internal herniation; NS-not specified; CT-CT scan

um (passive component) in a clockwise or anticlockwise direction. In type III, the ileocecal segment (active component) wraps itself around the sigmoid colon (passive component).[2,4] The most common type of ISK reported is type I (53.9% to 57.5%), followed by type II (18.9% to 20.6%), type III (1.5%), and others undetermined. The direction of torsion is clockwise in 60.9% to 63.2% of cases.[4,8,9] The torsion is 360° in 52.9%, 360°×2 in 19.1%, and 360°×3 in 5.9%.[4,8]

ISK can rapidly progress to gangrene of the ileum as well as of the sigmoid colon.[2,3,4] Generalized peritonitis, sepsis, and dehydration are the principal complications. The predominant symptoms and signs of presentation include abdominal pain and tenderness (100%), abdominal distension (94% to 100%), nausea and vomiting (87% to 100%), rebound tenderness (69%),[4] and shock (0% to 60%), where it was specified (Table 1).

Despite the critical condition, preoperative diagnosis is not easy. While in recent years a preoperative diagnosis has been made more often, it was a rarity in the past in most cases (0% to 28%). The diagnostic difficulty is partly caused by the unfamiliarity of this rare entity and the confusing and self-contradictory features of the disease. While clinical features such as vomiting suggest small bowel obstruction, the radiographic findings are that of colonic distension, which is uncommon in small bowel obstruction.[3,4,12] Radiographically, ISK is often mistaken for simple sigmoid volvulus. However, unlike sigmoid volvulus, attempts to deflate the distended colon using a sigmoidoscope or a flatus tube, often fails in ISK. This is because the ileum tightly envelops the base of sigmoid colon, defying any such attempt. These three features of the clinical picture of small bowel obstruction, radiographic evidence of predominately large bowel obstruction, and inability to insert a sigmoidoscope could possibly form a useful diagnostic triad.[12]

The radiographic findings of ISK, which include a double loop of dilated sigmoid shadow and multiple air fluid levels in the small intestine, are sporadically described and are difficult to identify as such because of unfamiliarity.[2,3,4,8,12] Nonetheless, it is important that they should at least raise the suspicion of ISK. The findings in a CT scan suggestive of ISK include the whirl sign created by the twisted intestine and sigmoid mesocolon in ileosigmoid knot, medial deviation of the cecum, and descending colon.[11,13,14] In addition,

Table 3. Surgical procedures and outcome.

Author	No.	IR+PA SD	IR+PA MS	IR+EI SR+PA	ID SR+PA	IR+PA SR+PA	IR+PA SR+HR/Col	Outcome	
								Good	Death
Bawa, 2008	1					1		1	
Atamanalp, 2006	9	1				1	7	8	1 (11.1%)
Berrebi, 2006	1						1	1	
Hirano, 2005	1					1		1	
Atamanalp, 2004	63	10	2	1		6	38	53	10 (15.9%)
Hashimato, 2004	2					2		2	
Tamura, 2004	1					1		1	
Raveenthiran, 2001	7				4	3		7	
Akgun, 1997	16	4	3	3	3	3		13	3 (18.7%)
Alver, 1993	68	10			18	26	33	47	21 (30.8%)
Miller, 1992	1					1		1	
Puthu, 1991	7					4	2	5	2 (28.7%) (1 on table)
Kakar, 1981	11	2	2				7	8	3 (27.2%)
Shephard, 1967	92							48	44 (47.8%)

IR-ileal resection; PA-primary anastomosis; SD-sigmoid colon detorsion; MS-mesosigmidostomy; EI-end ileostomy; HR-Hartman's procedure

others have noted radial distribution of the intestine and mesenteric vasculature and consider it to be helpful diagnostic information.[11] However, CT examination may not be possible in all patients as some could be in poor condition or because of nonavailability. Whenever possible, a CT examination could be useful in making a diagnosis in these otherwise difficult patients.[11,13,14]

The initial management involves aggressive resuscitation with fluid and electrolytes with the help of central venous pressure monitoring, if required, and the correction of acid-base imbalance if any. After hemodynamic stabilization, laparotomy should not be delayed. Appropriate antibiotic therapy is commenced early and continued after the operation. The usual antibiotic combination includes cephalosporins, aminoglycosides, and metranidazole.[5,7,12]

The anatomical and pathological changes dictate the operative procedure.[2-13] In 73.5% to 79.4% of the cases, gangrenous bowel was encountered, whereas in 20.6% to 26.5% both small and large bowel were assessed to be viable in surgery.[2,4] In 52.9% to 60.3% cases, both the small intestine and sigmoid colon were gangrenous.[2,4,8,9] Paradoxically, the incidence of bowel gangrene was 90.9% in those who presented within 24 hours of their symptoms. Among those who presented after 24 hours after their initial symptoms, bowel gangrene was seen in 57% (chi-squared 9.94, $P<.01$).[2,4]

Various surgical procedures have been conducted in these patients (Table 3). If both loops are viable the knot may be undone by sigmoid enterotomy and traction of the sigmoid loop. This procedure may also be selected when the sigmoid colon alone is viable. When the ileum and the sigmoid colon are gangrenous, it can be difficult to untie the knot, and rupture of the gangrenous loop could lead to spillage of toxic bowel contents.[3-6] Therefore, intestinal clamps should be applied before dissection or resection of the knot followed by resection of both the loops.

Primary anastomosis of the small bowel is preferable, but if the terminal ileum is gangrenous to within 10 cms of the ileocecal valve, an end-to-end anastomosis should not be attempted.[2-4] The distal stump should be closed and end-to-side ileocaecostomy should be performed. Resection of the sigmoid colon is often advised in all instances even when viable. Recurrent volvulus or repeat knotting due to redundancy of the loop may cause gangrene after surgery. In the past, a Hartmann operation or a covering colostomy was advocated to avoid the risk of fecal leak from colonic anastomosis. However, recent data suggest that primary colonic anastomosis may be undertaken safely when the history is short and the remaining bowel is clean, well vascularized and undistended.[11-15] Intraoperative colonic irrigation, followed by resection and primary anastomosis, is another alternative. Avoiding a colostomy is always welcome as it reduces the morbidity and cost of health care.[12] In patients without sigmoid gangrene, mesosigmoidostomy is practiced by some to prevent recurrent ISK.[5,6,8,9]

The reported mortality from ISK varies from 0% to 48% (mean, 35.5%) (Table 3). The mortality figures are generally related to the duration of symptoms, the presence or absence of gangrene and the general status of the patient, including the presence of septicemic shock.[2-9] However, some of the reports suggest that those patients who undergo surgery within 24 hours after the onset of symptoms have a significantly higher incidence of mortality than those whose symptoms exceed 24 hours.[2-4] In spite of early judgment for prompt surgical intervention, the higher rates of both gangrene and mortality seem paradoxical and presumably reflect the fulminating clinical deterioration of patients due to early and extensive infarction of the bowel involved in a tight knot. However, others have found no correlation between the duration of symptoms and incidence of gangrene and consider the incidence and onset gangrene to be related more to the geometric degree of rotation than the duration of symptoms.[12] The literature review reveals that there has been a constant decline in the mortality with few reported cases of adverse outcome in the last ten years (Table 3).

In summary, ISK is a rare cause of intestinal obstruction. Unfamiliarity and diagnostic difficulties have contributed to the high morbidity and mortality of this condition in the past. Better understanding of the problem, and increased probabilities of preoperative diagnosis with aid of CT scanning, have facilitated early diagnosis and intervention. Aggressive fluid resuscitation, preoperative antibiotics, prompt laparotomy, and effective surgery, including resection and primary anastomosis or mesosigmoidoplasty of viable sigmoid colon and better perioperative care of the shocked patient have optimized the survival of these patients.

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case report

Primary mediastinal hydatid disease leading to popliteal artery hydatid cyst embolization

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Ann Saudi Med 2009; 29(5): 407-409

Hydatid disease is a zoonosis caused by *Echinococcus granulosus*. Infected dogs release eggs through their feces and the eggs infect humans through food and water. The most common locations of hydatid cysts are the liver and lungs, but primary mediastinal involvement, though rare, can be encountered. We report on a 16-year-old female with a primary mediastinal hydatid cyst leading to popliteal arterial embolization. The mediastinal lesion was treated with partial pericystectomy with removal of the germinal membrane and prophylactic albendazole. In endemic areas, it is important to consider hydatid cysts in the differential diagnosis of an acute arterial occlusion.

Hydatid disease is an endemic disease in various geographical areas of world. The disease can involve almost every organ, though the liver and lung are common sites. Mediastial hydatid cysts, though rare, have been reported in literature.[1,2] These hydatid cysts can also result in arterial occlusions in the aorta, iliac arteries, femoral arteries, popliteal arteries and even the mycardial arteries.[3,4] We report a case of a primary mediastinal hydatid cyst in an adolescent leading to popliteal arterial embolization, in which the patient presented with a popliteal arterial hydatid cyst embolus. The primary cyst was seen on computed tomography in the mediastinum, eroding the descending thoracic aorta and an embolus with evidence of hydatid cyst componenets was found in the popliteal artery.

CASE

A 16-year-old Kashmiri female presented with pain in the left leg for 2 days. The pain was continuous in coarse and initially was localized to the lower calf and foot and then involved the whole leg. She had not had these symptoms before and had been previously healthy. On examination she had a pulse of 80/minute with body-temperature of 98.5°F. The left leg was tender and cold with absent dorsalis pedis and posterior tibial arterial pulses on palpation. Homans sign was negative. There was no sensory loss. Joint movements and deep tendon reflexes were normal. Her abdominal and chest examinations were unremarkable. Doppler ultrasonography showed a hypoechoic popliteal arterial embolus with echogenic linear areas (Figure 1). A membrane-like structure was removed by urgent catheter embolectomy. A provisional diagnosis of intravascular hydatid cyst, leading to embolization was made, which was confirmed on histopathology (Figures 2 and 3). Serum serology for hydatid disease by ELISA test was negative. Abdominal ultrasonography was unremarkable. Chest x-ray showed a small left-sided pleural effusion. A multislice CT scan of the chest showed a cystic laminated structure in relation to the wall of the aorta, primarily arising from the mediastinum and eroding the wall of the aorta. This lesion appeared to be communicating with the aorta (Figure 4). No other abnormality was detected in the abdomen or chest on CT scan. Partial pericystectomy with removal of the germinal membrane was done through a median sternotomy approach and the patient was placed on prophylactic albendazole to avoid recurrence. Postoperative period was uneventful and the patient was discharged after 10 days.

DISCUSSION

Hydatid disease is still a health problem in endemic areas of the world, especially in developing countries.[5] The infection known as hydatidosis is a zoonotic infection caused by *Echinococcus granulosus* belonging to the class Cestoda. The organism lives in the small intestine of definitive hosts such as canines.[6] Sheep and cattle are

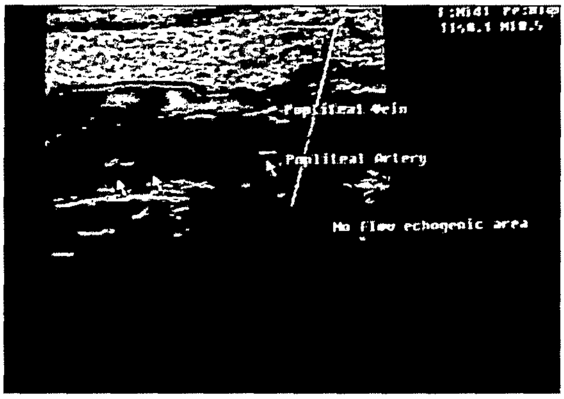

Figure 1. Popliteal artery embolus with linear echoic area within, with normal flow in the popliteal vein.

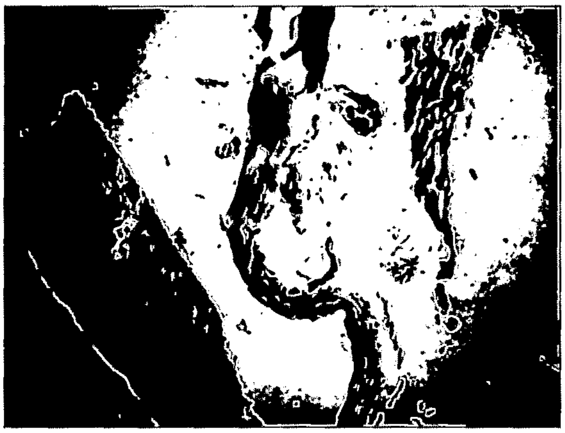

Figure 2. Photomicrograph showing laminated membrane of the hydatid cyst in an embolus.

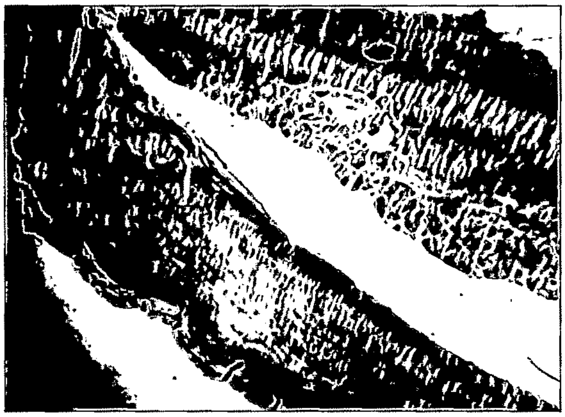

Figure 3. Another photomicrograph showing laminated membrane of the hydatid cyst in an embolus.

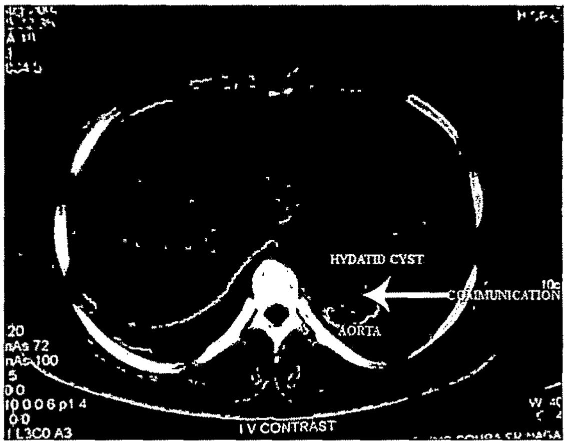

Figure 4. Transaxial contrast-enhanced multislice image showing posterior mediastinal hydatid cyst communicating with the aorta.

intermediate hosts and the echinococcal eggs enter the human body through food and water contaminated by the feces of infected canines. Children are not spared by this disease.[7] Due to unhygienic conditions in developing countries the chances of getting hydatidosis are greater and this disease can involve any organ. Though the most common involved organs are the liver and lungs, hydatid cysts are seen also in other parts of body.[8] The extrapulmonary and mediastinal involvement of hydatid cysts is rare.[9,10] The most common location in the mediastinum is the posterior mediastinum.[11] In one study of 1619 intrathoracic hydatid cysts, only 8 (0.5%) were found in the mediastinum.[12] Complications caused by hydatid cysts if vascular invasion develops include anaphylactic shock, hemorrhage, systemic emboli and arterial occlusion.[13] Marti-Bonmati et al documented a case on CT scan in which a hydatid cyst had ruptured into the aorta leading to bilateral popliteal embolism.[14]

The contrast-enhanced computed tomographic features represent a pathognomonic sign of a communicating rupture of an echinococcal cyst into the aorta.[14] This case strongly suggest that in endemic areas for hydatid disease, it is important to consider hydatid cysts in the differential diagnosis of acute arterial occlusion. Screening should be done to rule out hydatid cyst in other parts of body, especially in relation to large vessels and when there is no clear cause or risk factor for arterial occulsion such as in this case.

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images

Which one is the urinary bladder?

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· Accepted for publication May 2009

Ann Saudi Med 2009; 29(5): 410-411

An 85-year-old man complained of dysuria and nocturia for months and developed painless gross hematuria for 4 days. Physical examination showed a palpable, non-tender, distended mass 10 cm over the supra-pubic region. Digital rectal examination revealed moderate enlargement of the prostate without nodularity or tenderness. There was severe hematuria and pyuria on urinalysis. Sonography of the pelvis revealed a large cystic lesion 9.5 cm adjacent to the urinary bladder and a 0.25 cm small hole communicating between the cyst and the urinary bladder with a left-to-right jet phenomenon (Figure 1) suggestive of a large bladder diverticulum on the left lateral wall of the urinary bladder. A CT scan confirmed a bladder diverticulum with a smooth mucosal outline over the left side (Figure 2). Open diverticulectomy was refused by patient.

Urinary bladder diverticulum is an outpouching of the urothelium through the muscular layer; the diverticulum wall is constituted of the chorionic urothelium. Because there are no muscular fibers within the wall of the diverticulum, stasis leads to chronic inflammation and squamous metaplasia in about 80% of cases.[1-5] Benign prostatic hyperplasia may be a contributing factor in the development of a bladder diverticulum. Complications of bladder diverticulum include a draining defect, which is responsible for infections and a urothelial tumor in the cavity.

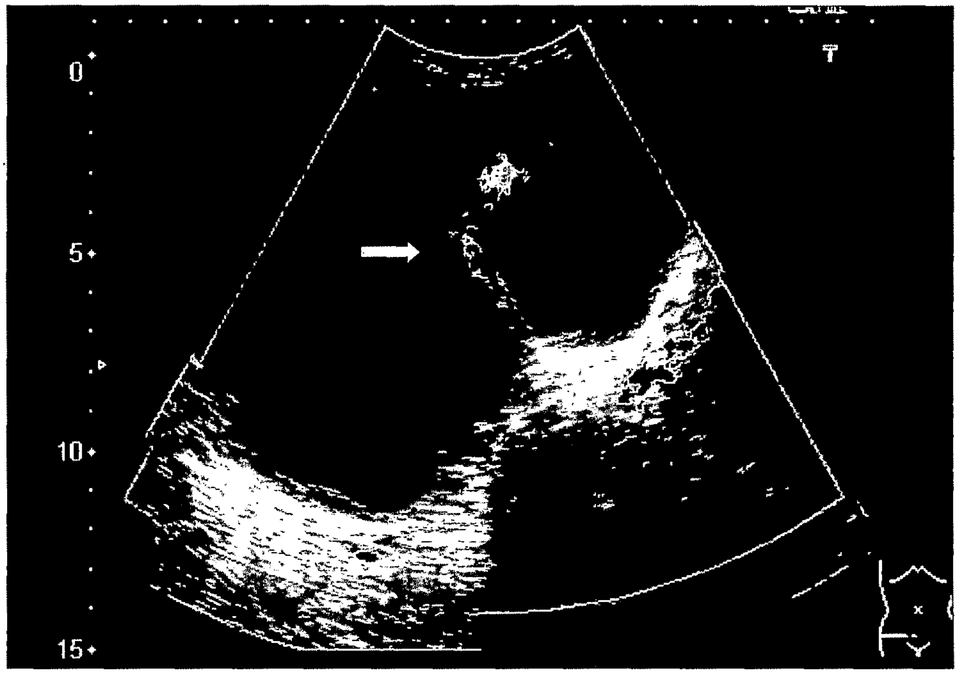

Figure 1. Sonography of the pelvis showing a large cystic lesion 9.5 cm in diameter (right) and a 0.25 cm small hole connecting the diverticulum (right) and the bladder (left) with a left-to-right jet phenomenon.

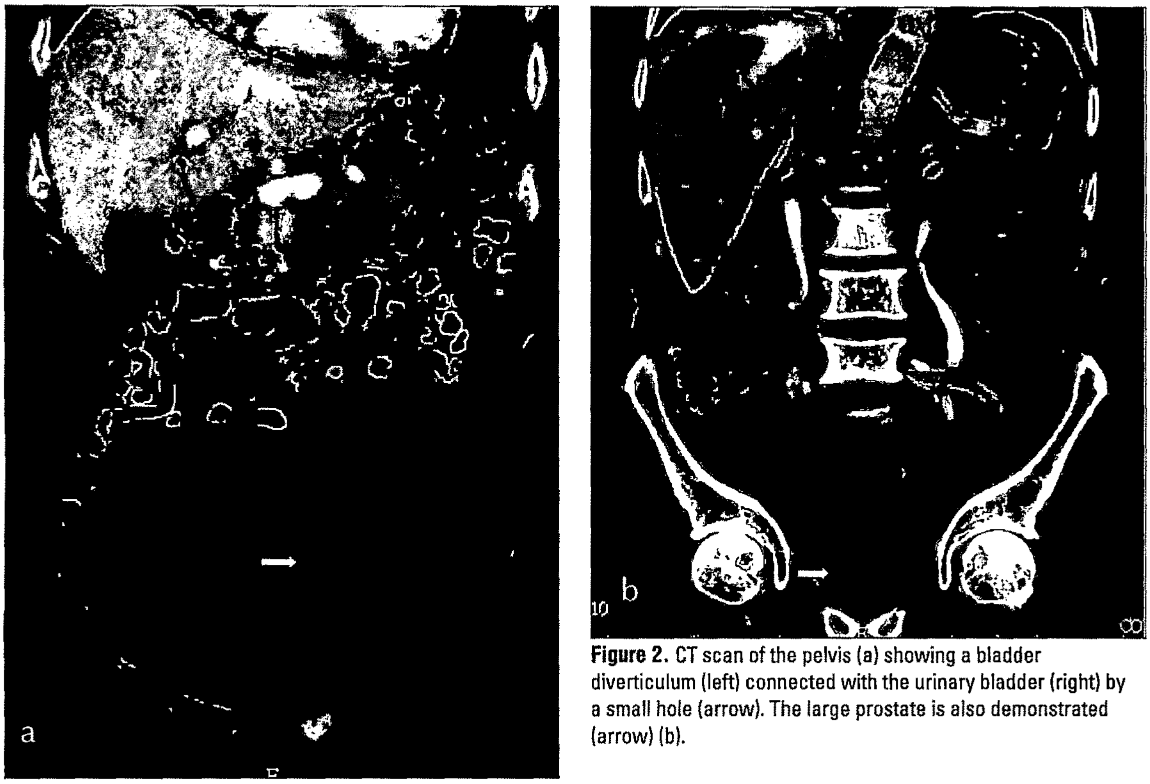

Figure 2. CT scan of the pelvis (a) showing a bladder diverticulum (left) connected with the urinary bladder (right) by a small hole (arrow). The large prostate is also demonstrated (arrow) (b).

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Priapism as the first manifestation of chronic myeloid leukemia

To The Editor: A previously healthy 33-year-old Moroccan man was referred to the local hospital for persistent painful erection of the penis that had lasted approximately 22 hours. His penis remained erect, painful, and swollen when he arrived at the emergency department. He denied recent intercourse, trauma, use of illicit drugs, use of medications, and radiation therapy. The patient also denied fever, sweats, and chills. The vital signs revealed a body temperature of 37.4 °C, pulse of 98 beats/minute, and blood pressure of 12/7 mm Hg, and respiration of 22 beats/minute. He was alert and oriented. The physical examination revealed that the spleen was palpable 4 cm below the left costal margin. His conjunctiva was pale but no jaundice. On examination, the penis was erect, firm, and tender with superficial venous engorgement. Urinalysis was normal. Laboratory data showed hemoglobin 10.53 g/dL, hematocrit 24%, white blood count 400 000/mm^3, and platelets 1 200 000/mm^3. A peripheral blood smear demonstrated immature leukocytes in various stages of differentiation. Karyotype analysis revealed the Ph1 chromosome and myeloid hyperplasia in the bone marrow. A diagnosis of chronic myeloid leukemia (CML) was made. Treatment of the priapism was initially performed by cavernosa aspiration and epinephrine irrigation at emergency department under the impression of low flow-type priapism. The erection was relieved later by these procedures. For hyperleukocytosis, the patient was admitted to the hematological ward. He was started on hydroxyurea therapy (50 mg/kg/day) associated with intravenous fluid hydration and allopurinol (300 mg/day) for potential tumor lysis syndrome. After 15 days of chemotherapy with hydroxyurea, the patient's leukocyte and platelet counts were 8 000/mm^3 and 240 000/mm^3, respectively. Recurrent priapism had not happened to him during his admission period. The patient was treated with imatinib mesylate for his CML and continued to report to us without any erectile dysfunction until the date of writing.

Priapism is a rare disease, characterized by prolonged, painful and irreducible erection, not resulting in ejaculation. It is an andrological emergency with a poor prognosis, as the risk of impotence is 50% despite appropriate management. Sickle cell anaemia, chronic myelogenous leukemia, chronic lymphocytic leukemia, and acute lymphoblastic leukemia are hematologic disorders that can be a cause of priapism.[1] In adult leukemic patients, the incidence of priapism is estimated to be approximately 5%.[2] Priapism as a result of hematologic malignancy is most likely caused by venous obstruction from microemboli/thrombi as well as hyperviscosity caused by the increased number of circulating leukocytes in mature and immature forms.[3] In cases of hematologic malignancy, controversy has existed regarding the optimal treatment of leukemic priapism. Earlier series of case reports show successful detumescence with local radiation therapy, open surgical shunting, or combination of the two treatments.[4] More recent literature has focused on the use of cytoreductive modalities such as chemotherapy or combination chemotherapy and leukapheresis.[5] Because of the relatively rare occurrence of leukemic priapism and the small number of case series, there is no standard treatment protocol. Chemotherapy or radiotherapy may first be attempted. If detumescence is not achieved, then surgical shunting should be considered.

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Is CCR5-Δ32 mutation associated with diabetic nephropathy in type 2 diabetes?

To the Editor: Immunological factors like the chemokine-receptor axis recently were proved to have crucial roles in diabetes and its complications.[1] CCR5 is a G-protein CC (CCL3, CCL4, CCL5) chemokine receptor, which recruits immune cells to the site of infection, inflammation and injuries, including nephropathic disease.[2] Previous studies demonstrated that a mutation in the unique exon (exon 1) of the CCR5 and deletion of 32 nucleotides (also known as Δ32) leads to decreased expression and function of CCR5.[2] Due to its immunomodulatory functions, the CCR5-Δ32 mutation seems to play a key role in autoimmune and inflammatory diseases.[3] This study aimed to analyze the CCR5-Δ32 mutation in type 2 diabetic patients with and without diabetic nephropathy (DN). Samples were collected from 100 type 2 diabetic patients with DN, 200 type 2 diabetic patients without DN and 300 healthy controls. The groups were of the same sex, roughly the same age, diabetes history and socioeconomic status. DNA extraction and Gap-PCR reactions were performed as our previous study.[4] Our findings indicated the absence of CCR5-Δ32 in type 2 diabetic patients with and without DN, while only two controls showed a heterozygotic pattern of mutation. A significant difference was not observed in the CCR5-Δ32 mutation in diabetic patients and controls ($P<.78$).

The CCR5 affects the immune cell function,[1] and thus, the CCR5-Δ32 mutation leads to decreased CCR5 expression and influences the function of these cells.[3] In agreement with our results, Kalev and colleagues reported a lack of association between CCR5-Δ32 mutation and DN in native Estonian type 2 diabetic patients.[2] Studies also demonstrated that type 1 diabetes is not related to CCR5-Δ32.[5,6] Like other investigators, we could not find any association between development of DN and CCR5-Δ32 mutation. Based on our findings and others, it seems that CCR5-Δ32 in diabetic type 2 patients is independent of geographical and ethnic factors. Prasad et al, showed that CCR5-Δ32 is not related to nephropatic type 2 diabetes in Asian-Indians.[7] Another study in type 1 diabetic patients with renal failure showed that male carriers with CCR5-Δ32 mutation had a higher risk of nephropathy.[8] To our knowledge none of research groups showed an association of CCR5-Δ32 with nephropathy in type 2 diabetic patients, but other CCR5 gene polymorphisms are associated with these nephropathies.[7,9] Overall, based on the results of this study and globally collected data, it is likely that the CCR5-Δ32 mutation is not associated with diabetes and the nephropathic complications of diabetes.

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Filariasis of the breast, diagnosed by fine needle aspiration cytology

To the Editor: Bancroftian filariasis has a worldwide distribution, with disease prevalence in Africa, Asia including China, India and Southeast Asia, the Caribbean islands, Central and South America.[1] It is a major health problem in tropical countries. The breast is an unusual site for the occurrence of a filarial nodule and only a few such cases have been documented.[2-5] Microfilariae (MF) and adult worms are detected by needle aspirates from the breast, which aid in the diagnosis and treatment of the disease. Other rare unusual sites in which MF are reported include the thyroid nodule,[6] salivary gland,[7] cervicovaginal smear,[8] ovarian cyst fluid,[8] bronchial brushings,[8] effusion fluid,[8] and gastric brush.[9]

A 29-year-old female presented at the Super Religare Laboratory (formerly SRL Ranbaxy) Gurgaon, India, with a complaint of a mass in the right breast for 3 months duration. On palpation, a small subcutaneous nodule of approximately 9 mm in diameter was identified in the areola. The nodule was firm and nontender. The overlying skin was normal. There was no nipple discharge and the axillary lymph nodes were not palpable. Other physical and medical examinations were unremarkable. Fine needle aspiration (FNA) of the breast nodule was performed using a 23-gauge needle attached to a 10 mL disposable syringe. The aspirate was smeared on a slide, air-dried, and stained with May-Grunwald-giemsa stain. Cytologic examination revealed a gravid female adult worm along with numerous MF both in coiled and uncoiled forms (Figure 1) The MF were sheathed with elongated terminal nuclei and a caudal space at the posterior end (Figure 2) There were scattered inflammatory cells comprising polymorphs, lymphocytes and few histiocytes. No ductal cells were included in the aspirated material. A diagnosis of MF of the breast morphologically consistent with the *Wuchereria bancrofti* was entertained. Since our establishment was a diagnostic laboratory, the patient was subsequently referred to the concerned physician for the treatment and follow-up, and we have no further information on her disposition.

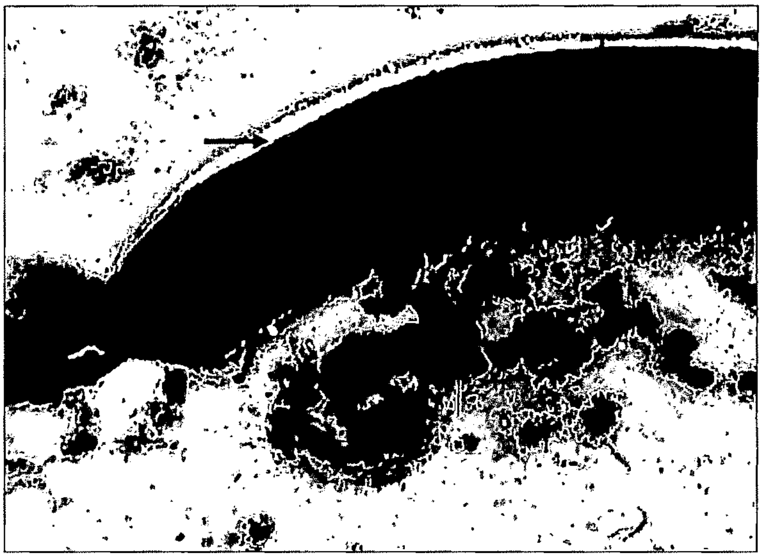

Figure 1. Aspirate showing female adult filarial worm (thick arrow) along with discharged numerous coiled form of larvae (thin arrow) outside the adult worm (May-Grunwald-giemsa stain ×100).

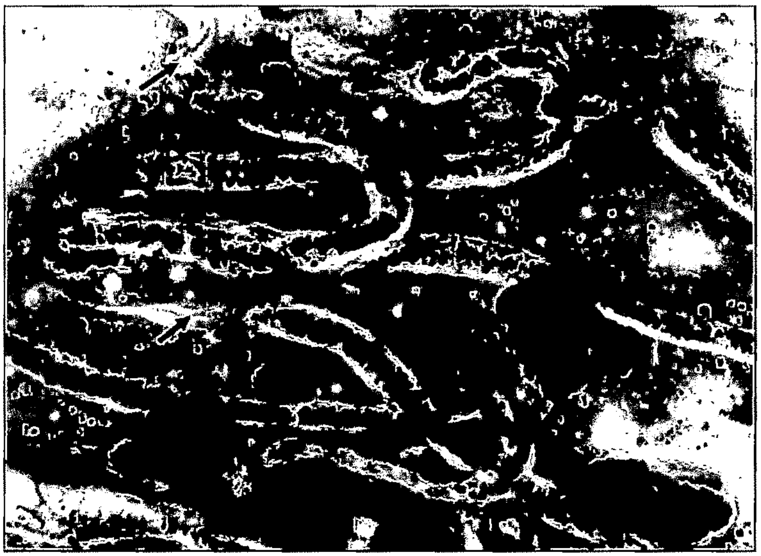

Figure 2. Microfilarial larvae showing sheathed, terminal nuclei and a caudal space (arrow) at the posterior end (May-Grunwald-giemsa stain ×400).

Bancroftian filariasis has a worldwide distribution. Insects, particularly mosquitoes serve as the intermediate host. While taking a blood meal, the insect ingests MF. Over 2 to 3 weeks, the MF develop within the insect into infective third-stage larvae. They reenter the definitive human host when the insect feeds again. The larvae mature into adult worm which lives for 10 to 15 years and produces MF. The patient usually presents with a solitary painless nodule in the upper outer quadrant of the breast. Central and periareolar regions are also involved with notable frequency as seen in our case. Multiple lesions are uncommon.[5] Most of the lesions manifest as subcutaneous hard mass nodule with cutaneous attachment. More recently, in endemic areas, FNA has been employed to diagnose cases of breast involvement.[2-5] In the present case, an FNA smear yielded a fragment of gravid female adult worm along with numerous MF. Cytologic diagnosis of filariasis by FNA from other sites, other than the breast such as the testis, epididymis, thyroid, lung, lymph node and skin, has been reported. A review of these cases by Kaya and colleagues revealed that the positivity for the MF in blood examinations in these patients was approximately 12%.[10] Therefore, because of the low yield and stringent sampling requirement of a blood examination, FNA cytology appears to be a more convenient and effective diagnostic method in patient with mass lesions. Thus to conclude, demonstration and identification of the parasite in the smear played a significant role in the prompt recognition of the disease and institution of specific therapy.

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Reply to Alavian and Tabatabaei: Serum viral markers in Iranian patients with congenital bleeding disorder

To the Editor: I appreciate the comments of Drs. Alavian and Tabatabaei on our article in the November-December 2008 issue of the *Annals*.[1] The HCV positivity rate of 40% mentioned in previous studies is related to a survey of hemophilic children aged under 12. The survey was conducted in the Clinic for Hemophilic Children, Tehran, Iran. The individuals concerned have taken coagulation factors and products after virus inactivation (after 1985). The study carried out at Imam Khomeini Hospital Tehran, Iran, and involved nearly 400 of the total hemophilic patients (adults or children) admitted there with HCV positivity of 80% to 85%.[2] The reason for the increase could be explained by the use of coagulation factors contaminated with pre-1985 HCV and the lower referral of hemophilic patients to Imam Khomeini Hospital due to the breakout of HIV and the patient's fear for other sources of infection. Hemophilic patients are exposed to the threat of infection with other viruses and society has to pay more attention to this undeniable fact.

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links for authors and reviewers

Good reporting of trials and observational studies: Related guidelines and initiatives

EQUATOR

EQUATOR <**http://www.equator-network.org**> (Enhancing the QUAlity of Trials and Other Research) The EQUATOR Network is a new initiative that seeks to improve the quality of scientific publications by promoting transparent and accurate reporting of
health research.

STROBE

STROBE **(STrengthening the Reporting of OBservational studies in Epidemiology)** is an international, collaborative initiative of epidemiologists, methodologists, statisticians, researchers and editors involved in the conduct and dissemination of observational studies.

CONSORT (Consolidated Standards of Reporting Trials), is part of a broader push to produce reporting guidelines (RGs) for many different types of research. The main product of CONSORT is the CONSORT Statement, which is an evidence-based, minimum set of recommendations for reporting RCTs. It offers a standard way for authors to prepare reports of trial findings, facilitating their complete and transparent reporting, and aiding their critical appraisal and interpretation. The CONSORT Statement comprises a 22-item checklist and a flow diagram, along with some brief descriptive text.

ASSERT

The ASSERT **(A Standard for the Scientific and Ethical Review of Trials)** initiative is a proposed standard for the review and monitoring of randomized clinical trials by research ethics committees. Among other items, its checklist incorporates certain elements of CONSORT, to ensure fulfillment of the requirements for scientific validity in the ethical conduct of clinical research.

MOOSE

The MOOSE **(Meta-analysis of Observational Studies in Epidemiology)** paper reports the outcome of a 1997 workshop to examine the reporting of meta-analyses of observational studies. It makes recommendations to aid authors, editors, reviewers and readers of observational research.

QUOROM

The QUOROM **(Quality Of Reporting Of Meta-analyses)** conference resulted in the creation of the QUOROM Statement, which consists of a checklist and flow diagram.

STARD

The STARD **(Standards for Reporting of Diagnostic Accuracy)** initiative aims to improve the accuracy and completeness of reporting of studies of diagnostic accuracy in order to allow readers to assess the potential for bias in a study and to evaluate the generalisability of its results.

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The *Annals of Saudi Medicine* is published bimonthly by King Faisal Specialist Hospital & Research Centre. Arabic abstracts are prepared, in association with Dr. M. Zuheir Al-Kawi, by the staff of the Office Services Department of King Faisal Specialist Hospital & Research Centre.

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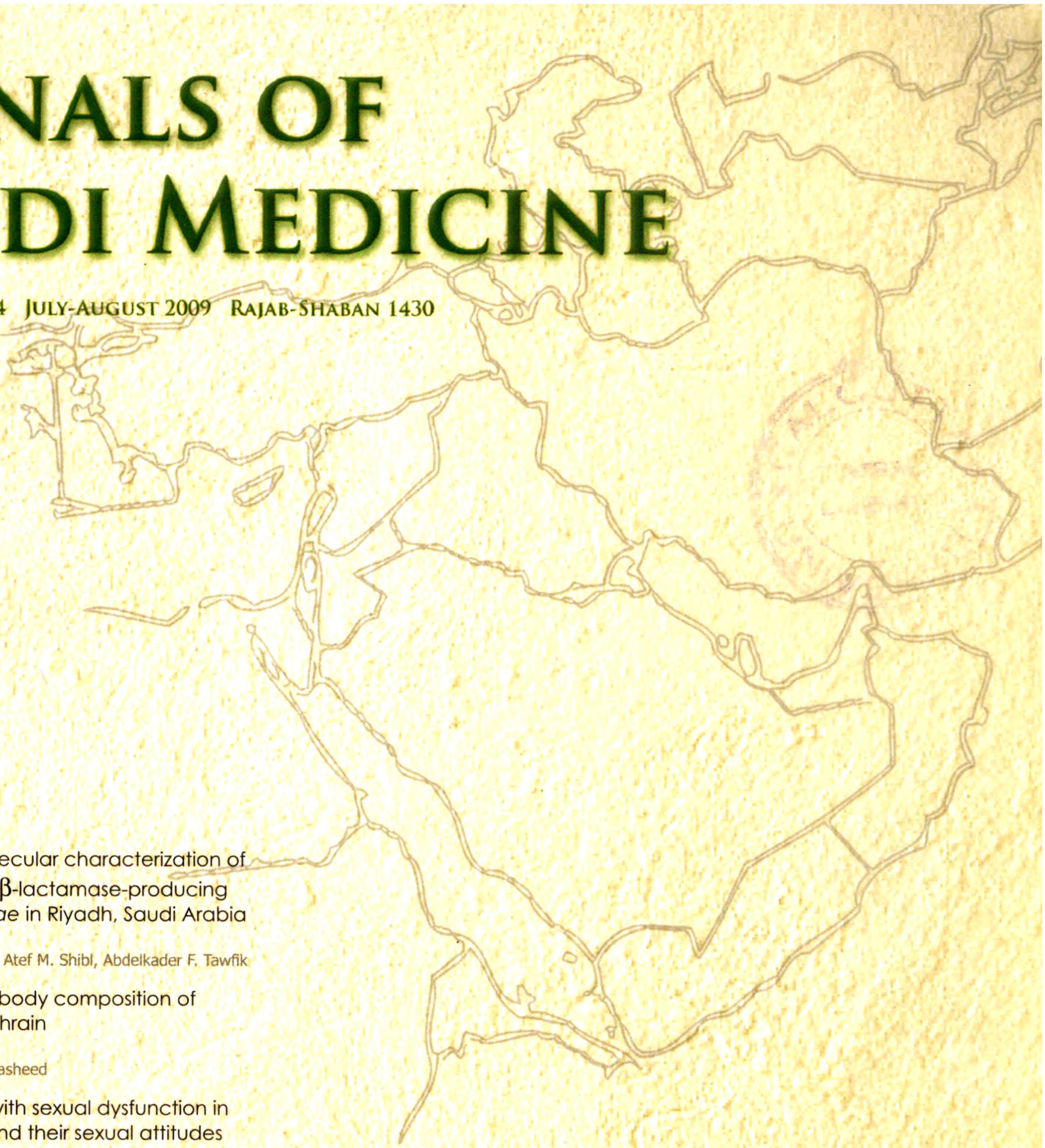

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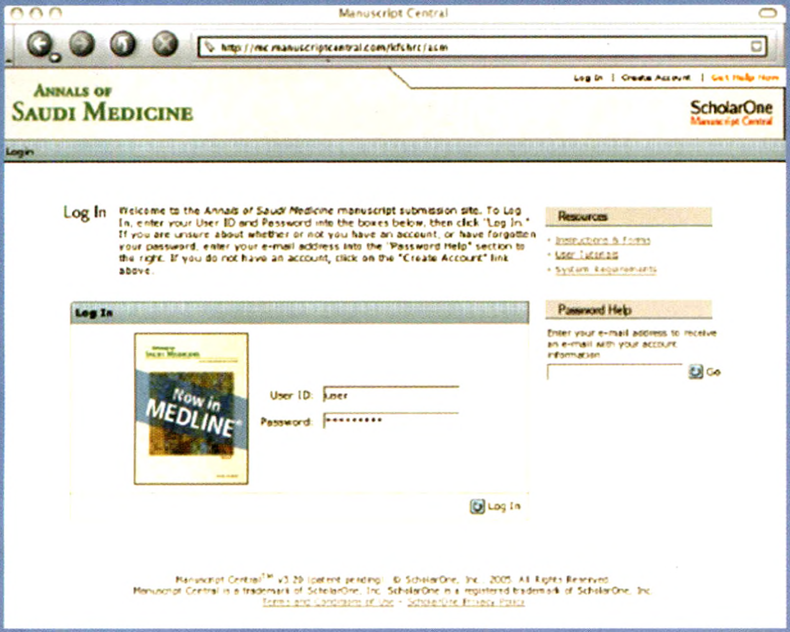

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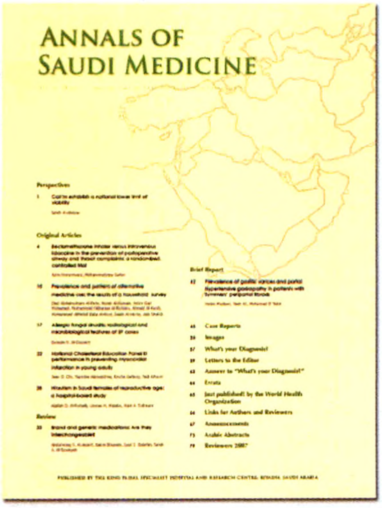

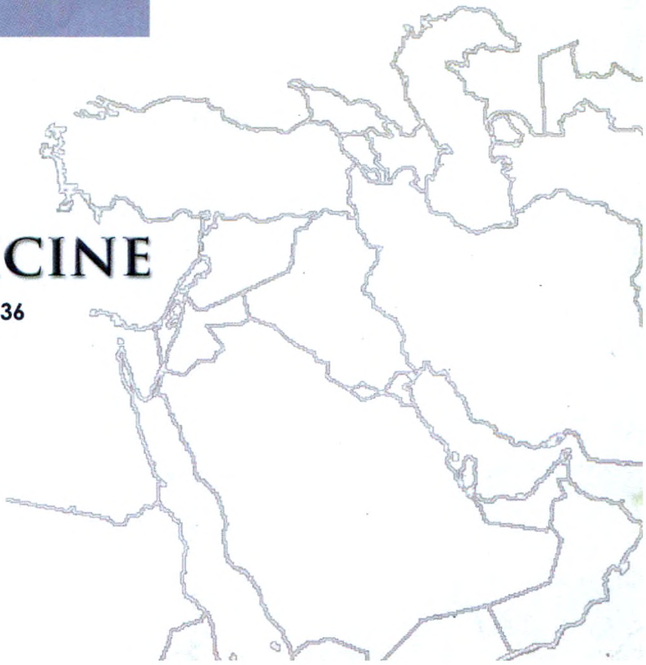

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مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة

Academic & Training Affairs
CME Section

SYMPOSIA

International Congress on Liver Diseases and Liver Transplant
03-04 March 2009 / 06-07 Rabi Al Awal 1430
Contact No. 4647272 Ext. 31830

ilding Connections for Global Nursing:Engage, Empower, Transform
27-28 October 2009 / 08-09 Dhu Al Qada 1430
Contact No. 4647272 Ext. 31830

The Health Consequences of Global Warming
06-07 October 2009 / 17-18 Shawwal 1430
Contact No. 4647272 Ext. 31912

Allergy, Asthma and Clinical Immunology Symposium
17-18 November 2009 / 29-30 Dhu Al Qada 1430
Contact No. 4647272 Ext. 31912

ORKSHOPS

e Art of Ultrasound Scanning in Fetal Care
-22 January 2009 / 23-25 Muharram 1430
ntact No.: 4427392 **Ob-Gyn**

diation Safety in Medicine
-29 January 2009 / 01-03 Safar 1430
ntact No.: 4647272 Ext. 32851 **Research Center**

diatric Infectious Diseases Seminar
-18 February 2009 / 22-23 Safar 1430
ntact No.: 4427798 **Pediatrics**

orkshop on Updates in Obstetric & Regional Anesthesia
-25 March 2009 / 27-28 Rabi Al Awal 1430
ntact No.: 464727 Ext. 32700 **Anesthesiology**

d Cleft Lip & Palate Workshop
March – 02 April 2009 / 04-06 Rabi Al Thani 1430
ntact No.: 4427651 **Dentistry**

scular Access in Dialysis Patient Workshop
-05 April 2009 / 08-09 Rabi Al Thani 1430
ntact No.: 4427752 **Surgery**

lvances in Wound Care
-29 April 2009 / 03-04 Jumada Al Awal 1430
ntact No.: 4427752 **Surgery**

ncer Cytogenetics Workshop
-27 May 2009 / 02-03 Jumada Al Thani 1430
ntact No.: 4647272 Ext. 35845 / 35861 **Pathology & Laboratory Medicine**

e Future of Healthcare for Adolescents in Saudi Arabia Seminar
-05 November 2009 / 15-17 Dhu Al Qada 1430
ntact No.: 4427761 / 4427763 / 4427765 **Pediatrics**

h Annual AIDS Workshop
-09 December 2009 / 21-22 Dhu Al Hijja 1430
ntact No.: 4427492 **Medicine**

hical Issues in Genetics: Clinical, Research & Treatment
-16 December 2009 / 28-29 Dhu Al Hijja 1430
ntact No.: 4424988 **Medical Genetics**

COURSES

4th Antimicrobial Review Course
17-18 March 2009 / 20-21 Rabi Al Awal 1430
Contact No.: 4647272 Ext. 38628 **Antimicrobial Utilization Evaluation**

7th Pediatric Intensive Review Course
26 Sep – 01 Oct 2009 / 07-12 Shawwal 1430
Contact No.: 4427763 **Pediatrics**

Internal Medicine Saudi Board Review Course
10-14 October 2009 / 21-25 Shawwal 1430
Contact No.: 4427495 **Medicine**

Projected Materials in Internal Medicine Course
15 October 2009 / 26 Shawwal 1430
Contact No.: 4427495 **Medicine**

ACADEMIC DAYS

King Faisal Cancer Centre Academic & Research Day
06 May 2009 / 11 Jumada Al Awal 1430
Contact No.: 4647272 Ext 38005 **KFCC**

11th Annual Research Celebration Day
12 May 2009 / 17 Jumada Al Awal 1430
Contact No.: 4427490 **Medicine**

7th Annual Academic Day
20 May 2009 / 25 Jumada Al Awal 1430
Contact No.: 4423934 **Pediatric Hematology / Oncology**

9th Annual Surgical Research & Residents Day
09 November 2009 / 21 Dhu Al Qada 1430
Contact No.: 4427776 **Surgery**

FOR INFORMATION

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Academic & Training Affairs, CME Section MBC 36
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Email: web-symposia@kfshrc.edu.sa
Website: www.kfshrc edu sa/symposia

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الشؤون الأكاديمية والتدريب
Academic & Training Affairs

Residency Training Programs

Saudi Specialty Certificate Programs

Anesthesiology
Dermatology
Dentistry
Emergency Medicine
General Surgery
Internal Medicine
Neurology
Neurosurgery
Obstetrics & Gynecology
Orthopedic Surgery
Otorhinolaryngology Head & Neck Surgery
Pathology
Pediatric Neurology
Pediatrics
Plastic Surgery
Psychiatry
Radiology
Urology

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Academic & Training Affairs
T: (966-1) 442-7214/442-7215
F: (966-1) 442-7237
or visit:
www.kfshrc.edu.sa/aape/residency.html

Fellowship Training Programs

Anesthesiology
- Cardiac Anesthesia*
- Pain Management
- Pediatric Anesthesiology*

Emergency Medicine
- Pediatric Emergency Medicine*

King Faisal Cancer Center
- Hematology*
- Medical Oncology
- Palliative Care

King Faisal Heart Institute
- Cardiology*
- Pediatric Cardiology*

Liver Transplantation & Hepatobiliary-Pancreatic Surgery
- Hepatobiliary-Pancreatic Surgery

Medical Genetics
- Medical Genetics

Medicine
- Critical Care Medicine*
- Endocrinology & Metabolism*
- Gastroenterology*
- Infectious Diseases*
- Nephrology*
- Pulmonary Medicine*
- Rheumatology*

Neurosciences
- Epilepsy and EEG
- Pediatric Neurological Surgery

Obstetrics & Gynecology
- Gynecological Oncology
- Maternal Fetal Medicine
- Reproductive Medicine

Orthopedic Surgery
- Musculoskeletal Surgical Oncology
- Pediatric Orthopedics
- Reconstructive Surgery

Otalaryngology, Head & Neck Surgery and Communication Sciences
- Head and Neck Surgery

Pathology
- Anatomic Pathology
- Hematological Pathology

Pediatrics
- Allergy and Clinical Immunology
- Pediatric Gastroenterology, Hepatology & Clinical Nutrition*
- Pediatric Endocrinology & Diabetes*
- Pediatric Infectious Diseases*
- Pediatric Intensive Care*
- Pediatric Nephrology*
- Pediatric Rheumatology
- Neonatal/Perinatal Medicine*

Pediatric Hematology/Oncology
- Pediatric Hematology/Oncology

Radiology
- Body Imaging
- Interventional Radiology
- Musculoskeletal Imaging
- Neuroradiology
- Nuclear Medicine
- Pediatric Radiology
- Woman Imaging

Renal Transplant Unit
- Renal Transplantation

Surgery
- Colorectal Surgery
- Endocrine & Breast Surgery
- General & Minimally Invasive Surgery
- Pediatric Surgery*
- Renal Transplant Surgery

Urology
- Pediatric Urology*
- Urological Surgical Oncology

**Saudi Subspecialty Certificate Program*

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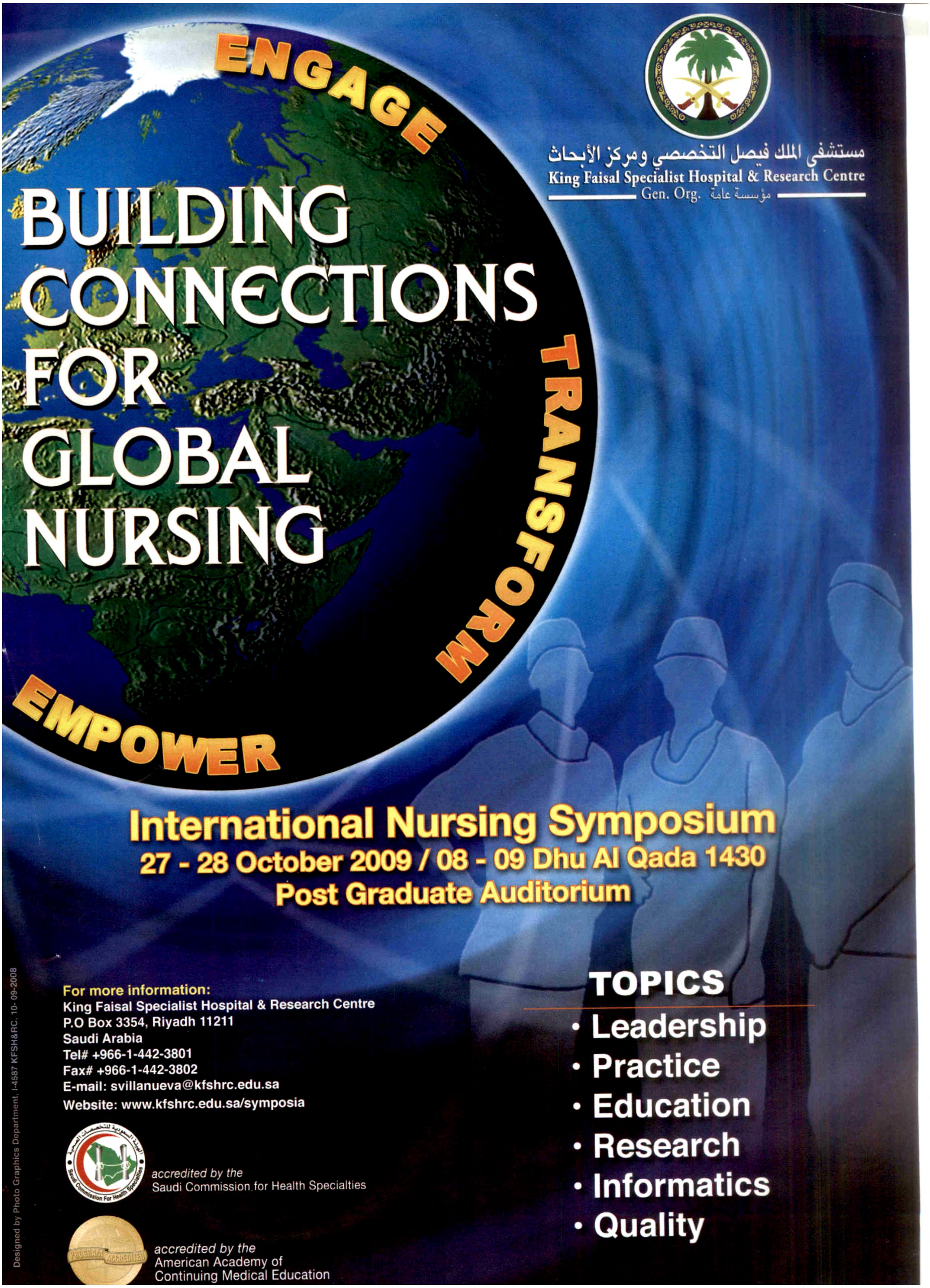

BUILDING CONNECTIONS FOR GLOBAL NURSING

International Nursing Symposium

27 - 28 October 2009 / 08 - 09 Dhu Al Qada 1430
Post Graduate Auditorium

For more information:
King Faisal Specialist Hospital & Research Centre
P.O Box 3354, Riyadh 11211
Saudi Arabia
Tel# +966-1-442-3801
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TOPICS

- Leadership
- Practice
- Education
- Research
- Informatics
- Quality

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King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة
Department of Pediatrics

The Future of Healthcare for Adolescents in Saudi Arabia

03- 05 November 2009 (15- 17 Dhu Al Qadah 1430)

INTERNATIONAL SPEAKERS

Prof. Martin Grabois'
Professor and Chairman of the Department of Physical Medicine and Rehabilitation
Professor of Anesthesiology at Baylor College of Medicine, Houston, Texas.
Adjunct Professor of the Department of Physical Medicine and Rehabilitation at the University of Texas Health Science Center Houston.

Lectures:
1. Pediatrics and Adolescents Rehabilitation Medicine Service: Development, Implementation, and Expansion
2. Functional Restoration in Patients with Chronic Pain
3. Multidisciplinary Pain Program for Evaluation and Treatment of Chronic Pain
4. Post Spinal Cord Injury and Treatment.

Prof. David Lau
President, Obesity Canada
Professor of Medicine, Biochemistry & Molecular Biology, Julia McFarlane Diabetes Research Centre
Chair, Diabetes and Endocrine Research Group, University of Calgary, Canada

Lectures:
1. Morbid Obese Adolescents: Who is Obese and Why?
2. Clinical Practice Guidelines on the Management and Prevention of Obesity in Adolescents
3. Long-Term Pharmacotherapy for Obesity and Overweight
4. Hyperlipidemia and diabetes in adolescent

Prof. Charles E. Irwin, Jr.
Professor and Vice Chairman of Pediatrics
Director, Division of Adolescent Medicine, University of California, San Francisco School of Medicine, San Francisco, USA

Lectures:
1. Approach to the unique care for adolescent
2. Risky behaviors during adolescents
3. Chronic illness in the adolescents
4. Improving Adolescent Health

Prof. Patricia Simmons
Chair, Board of Regents, University of Minnesota
Chair, Division of Pediatric and Adolescent Gynecology, Mayo Clinic
Professor of Pediatrics, Mayo Clinic College of Medicine, Minnesota, USA

Lectures:
1. Menstrual Disorders in Adolescents and adolescents with disability
2. Amenorrhea in adolescents
3. Polycystic Ovary diseases in adolescents

Prof. Albert Hergenroeder
Professor of Pediatrics
Head of Adolescent Medicine and Sports Medicine Section,
Baylor College of Medicine, Houston, Texas
Chief, Adolescent Medicine Service and Clinic, Chief,
Sports Medicine Clinic and Young Women's Clinic
Texas Children's Hospital, Texas, USA

Lectures:
1. Transition for youth and young adults with special healthcare needs from pediatric to adult based care.
2. Chronic Fatigue in Adolescents.
3. Common Sports Medicine

The Future of Healthcare for Adolescents in Saudi Arabia

VENUE:
Postgraduate Centre Auditorium
King Faisal Specialist Hospital & RC

WHO SHOULD ATTEND:
Pediatricians | Family practice physicians | Internist
Nurse Practitioners | Adolescents Medicine Specialists
Physical Therapists | Social Workers
Pharmacists | Healthcare Providers
Other Health care providers

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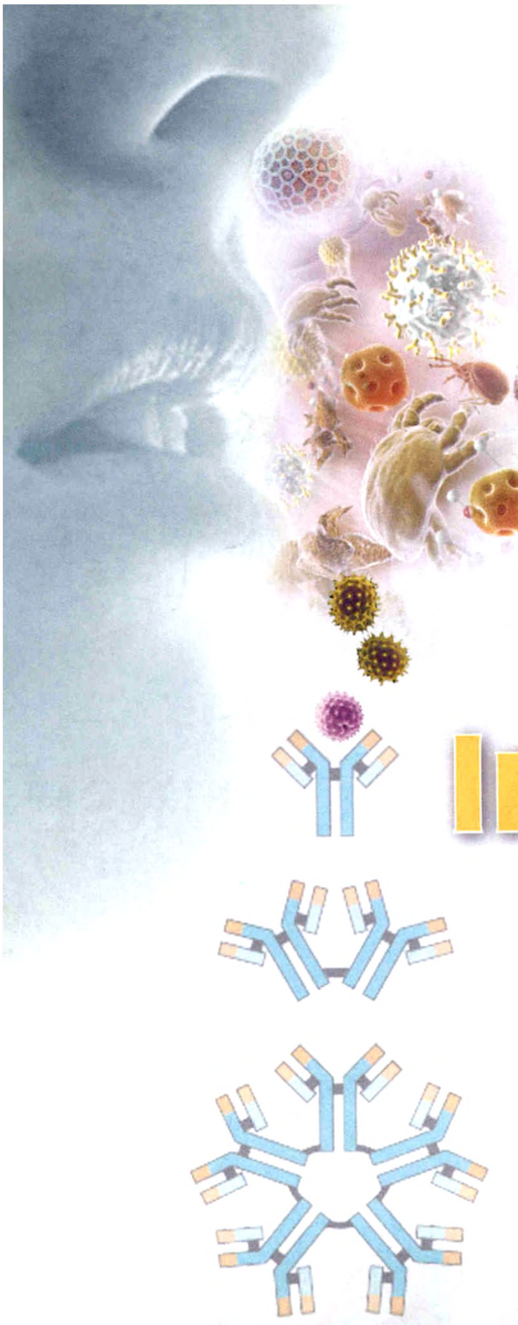
E-mail: mbernardo@kfshrc.edu.sa
Website Add: www.healthcareadolescents.com



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Allergy Asthma & Clinical Immunology SYMPOSIUM

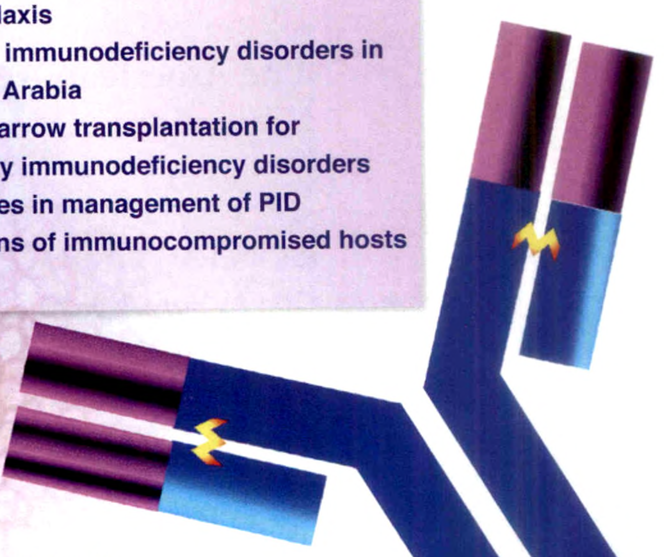
17-18 November 2009
29-30 Dhu Al Qada 1430

TOPICS

- Asthma
- Epidemiology of allergic diseases
- Allergic Rhinitis
- Role of immunotherapy in allergic diseases
- Food allergy
- Urticaria
- Atopic dermatitis
- Anaphylaxis
- Primary immunodeficiency disorders in Saudi Arabia
- Bone marrow transplantation for primary immunodeficiency disorders
- Advances in management of PID
- Infections of immunocompromised hosts

WHO SHOULD ATTEND

Pediatricians
Internists
General Practitioner
Allergists and Immunologists
Family Practice Physicians
Nurse Practitioner
Pharmacists
Respiratory Care Therapist
Health Care Providers
Other Allied Health Professionals



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CENTRE FOR CLINICAL STUDIES AND EMPIRICAL ETHICS
KING FAISAL SPECIALIST HOSPITAL AND RESEARCH CENTRE

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Centre for Clinical Studies and Empirical Ethics

11th SEMIANNUAL CLINICAL RESEARCH PROFESSIONALS' COURSE

05 to 16 Dhu Al-Qada 1430
24 October to 04 November 2009

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DEADLINE FOR REGISTRATION:
26 Ramadan 1430
16 September 2009

انتشار الآفات الفمية لدى مرضى طب الأسنان السعوديين

مقدمة: سبق أن أجريت عدة دراسات على مرضى سعوديين حول الآفات الفمية في الغشاء المخاطي، لكن الهدف من هذه الدراسة هو تقييم نوع الآفات الفمية ومدى انتشارها من خلال دراسة مقطعية مستعرضة أجريت على مرضى عيادة الأسنان في كلية طب الأسنان بالمملكة العربية السعودية.

المرضى والطرق: تمت معاينة ٢٥٥٢ مريضاً في العيادات الخارجية وفحصهم سريرياً على مدى ٣ سنوات، للكشف عن حالة الغشاء المخاطي الفمي لديهم، وقد تم أخذ تاريخهم الطبي وأجرينا فحص سريري فمي تام شمل التصوير الإشعاعي، وتسجيل نوعية الغشاء المخاطي الفمي وحالته.

النتائج: وجدنا أن ٣٨٣ من المرضى (١٥٪) يعانون من آفات مخاطية فمية، منهم ٥٧,٧٪ من الإناث أي (٢٢١ مريضة) و٤٢,٣٪ من الذكور (١٦٢ مريضاً). وتتراوح أعمار المرضى بين ١٥ إلى ٧٣ عاماً ويصل متوسط أعمارهم إلى ٣٨,٢ عاماً. وكانت أكثر مجموعة من الأعمار المصابة بالآفات بين ٣١ إلى ٤٠ عاماً التي تشكل ٢١,٤٪ (٨٢ مريضاً) من بين المصابين. أما أقل نسبة مجموعة من المصابين كانت ممن تزيد أعمارهم عن ٦١ عاماً. أكثر الآفات شيوعاً كانت من نوع حبيبات "فورديس" بنسبة (٣,٨٤٪ أي ٩٨ مريضاً)، تلتها الوذمة البيضاء بنسبة (٣,٣٧٪، ٨٦ مريضاً) أما الآفات الرضية (التقرحات والتآكل) فكانت بنسبة ١,٨٨٪ أي ٤٨ مريضاً. كما ظهرت شذوذات في اللسان بنسبة ٣,٩٦٪ (١٠١ مريضاً) من بين جميع الحالات التي أجريت عليها الدراسة، بحيث تتراوح بين ١,٤١٪ (٣٦ مريضاً) أصيبوا بانشقاق اللسان إلى ٠,٠٨٪ (مرضين) أصيبا باللسان المشروط. وكشفت نتائج أخرى أن نسبة المصابين ببروز البلاتونوز كانت (١,٣٣٪، ٣٤ مريضاً) وظهرت النتوءات المستديرة بنسبة (٠,٠٨٪ أي مريضين) وكانت نسبة التقرح القلاعي (٠,٣٩٪ أي ١٠ مرضى). وظهر الهربز البسيط بنسبة (٠,٢٧٪، ٧ مرضى) وفرط التقران الناجم عن الاحتكاك بنسبة (٠,٩٠٪، ٢٣ مريضاً)، والتملن نسبته (٠,٥٥٪، ١٤ مريضاً) أما الحزاز المسطح فكانت نسبته (٠,٣٥٪، ٩ مرضى) والتهاب الفم النيكوتيني بـ(٠,٥١٪، ١٣ مريضاً).

الاستنتاج: أوضحت نتائج هذه الدراسة معلومات مهمة كانت غير متوفرة سابقاً حول نوعية الآفات الفمية ومدى انتشارها بين مرضى طب الأسنان السعوديين، فهي توفر بيانات قاعدية للدراسات المستقبلية التي ستجرى عن انتشار الآفات الفمية بين السكان.

انفصال شبكية الأطفال في المنطقة الشرقية في السعودية: المعلومات من مستشفى رعاية متخصصة للعيون

مقدمة: نظراً لعدم إجراء أي دراسات سابقة حول هذه المشكلة، قمنا بوصف السمات السريرية والنتائج الجراحية لأطفال يعانون من انفصال الشبكية التشرمي المنشأ في المنطقة الشرقية في السعودية.

المرضى والطرق: أجرينا مراجعة استعادية على مدى ٣ سنوات لحالات متتابعة لأطفال بين (٠-١٨)سنة يعانون من انفصال الشبكية التشرمي المنشأ يراجعون في مستشفى الظهران التخصصي للعيون في المنطقة الشرقية.

النتائج: شملت الدراسة ٢٠ مريضاً، وهو ما يمثل ٩،٤٪ من جميع حالات جراحة انفصال الشبكية التي أجريت على مدى ٣ سنوات. وكان متوسط العمر ٨،٧. كانت حوادث الإصابات وقصر البصر/ التنكس الزجاجي الشبكوي وجراحة العين جميعها عوامل خطر واضحة لانفصال الشبكية التشرمي المنشأ. وجدت المقاومة الوعائية الرئوية فوق المرحلة "ج" في ٢٠/١٤ (٧٠٪) من الحالات. وقد تم علاج أغلب المرضى (٢٠/١٥، ٧٥٪) عن طريق استئصال الجسم الزجاجي الأملس ووضع حزام محيط حوله، في حين تم استخدام زيت السيلكون أو الغاز كدحس في ٢٠/١٣ (٦٥٪) من المرضى. نجحت العملية في ٢٠/١٧ (٨٥٪) من الحالات حيث نجحت في إعادة توصيل الشبكية. تحسنت حدة البصر بشكل واضح بعد العملية. أما في حالة انفصال الشبكية التشرمي المنشأ لفترة أطول والانتشار البقعي، فقد كانت نتائجها التشريحية أسوء بعد العملية الجراحية.

الاستنتاج: كثيراً ما يرتبط انفصال الشبكية التشرمي المنشأ في الأطفال في المنطقة الشرقية مع الأمراض المؤهبة. نجحت العملية في إعادة التوصيل التشريحي للشبكية في أغلب الحالات مع حدوث تحسن في حدة البصر.

انتشار المتلازمة الإستقلابية وعوامل الخطر القلبية الوعائية في الأطفال والمراهقين السعوديين الذين يعانون من السمنة: دراسة في مستشفى

مقدمة: قمنا بتقييم توزيع عوامل الخطر المرتبطة بالمتلازمة الإستقلابية في مجموعة من الأطفال والمراهقين السعوديين البدناء أو (البدينين). لم تتطرق أي دراسة سابقة حول هذه المشكلة في الأطفال السعوديين.

المرضى والطرق: تم تقييم ٥٧ طفل ومراهق سعودي بدين، مع متوسط عمر ٩,٨ (± ٣,٥) سنوات، بين عامي ٢٠٠٤م و ٢٠٠٨م. وقمنا بمراجعة سجلاتهم الطبية وجمع معلومات عن العمر، الوزن، الطول، مؤشر كتلة الجسم، ضغط الدم، تحليل دهون الصائم، غلوكوز الصائم وتركيزات الأنسولين. تم تقدير درجة مقاومة الأنسولين من خلال نتيجة نموذج تقييم الاستتباب لمقاومة الأنسولين.

النتائج: كان متوسط الوزن و مؤشر كتلة الجسم ٦٣,٧ (± ٢٨,٣) كيلوغرام و٣١,٦ (± ٨,٠) كيلوغرام/م على التوالي. عانى ٢٤ شخص (٤٢٪) من بين ٥٧ من ارتفاع ضغط الدم الانقباضي. ومن بين ٣٩ طفل خضعوا لتحليل الدهون، ١٠ منهم عانوا من فرط ثلاثيات الغليسريد في الدم، ٨ عانوا من فرط كولسترول الدم ، ٦ عانوا من ارتفاع في مستويات كولسترول البروتين الشحمي الخفيف الكثافة، و٦ عانوا من انخفاض مستويات كولسترول البروتين الشحمي الرفيع الكثافة. كما تم اكتشاف خلل في نتيجة الغلوكوز الصائم في ١٠ من بين ٣٨ من المرضى، وعانى ٩ من بين ٢٥ من المرضى من فرط الأنسولينية الصائم. انطبق تشخيص المتلازمة الاستقلابية على ١١ من بين ٣٧ من المرضى (٢٩,٧٪). ارتبط ضغط الدم الانبساطي ايجابياً مع مؤشر كتلة الجسم (r = ٠,٤٤٠, p = .٠٠١)، و ارتبط كولسترول البروتين الشحمي الرفيع الكثافة سلبياً مع الوزن و مؤشر كتلة الجسم (r = ٠,٤٨٧, p = .٠٠٢, r = ٠,٣١٧, p = .٠٥). ارتبط نموذج تقييم الاستتباب لمقاومة الأنسولين ايجابياً مع مؤشر كتلة الجسم ومستويات ثلاثي الغليسريد وارتبط سلبياً مع مستويات كولسترول البروتين الشحمي الرفيع الكثافة.

الاستنتاج: يعاني الأطفال والمراهقين السعوديين الذين يعانون من السمنة من عوامل خطر متعددة متعلقة بالمتلازمة الإستقلابية. انطبق على ٣٠ ٪ على الأقل من الأطفال والمراهقين السعوديين في دراستنا تشخيص المتلازمة الإستقلابية.

تباينات مناطقية في النمو عند الأطفال والمراهقين السعوديين

مقدمة: لم يسبق للدراسات أن وفرت بيانات حول التباينات المناطقية في النمو عند السعوديين، ولذا سعينا لدراسة الفروقات في النمو عند الأطفال والمراهقين السعوديين في مناطق المملكة المختلفة.

المرضى والطرق: تُمثل هذه الدراسة تحليلاً فرعياً للدراسة المرجعية لعام ٢٠٠٥م، والتي قامت على عينة تمثيلية عرضية للأطفال والمراهقين السعوديين الأصحاء منذ زمن الولادة وحتى سن ١٩ عاماً. فقد تم أخذ قياسات الطول والقامة والوزن ومحيط الرأس وإحتساب منسب كتلة الجسد وفقاً للتوصيات الإعتيادية. كما تم إنشاء مناسب بإستخدام طريقة LMS، تلاها تحويل كافة البيانات الفردية إلى منحنيات معيارية. وتم العمل على تطوير منحنى الوزن بالنسبة للسن، والطول بالنسبة للسن، والوزن بالنسبة للطول، ومحيط الرأس للأطفال من صفر وحتى ٣ سنوات، والوزن بالنسبة للسن، والقامة بالنسبة للسن، ومحيط الرأس ومنسب كتلة الجسد للأطفال من ٢ إلى ١٩ سنة. وتم بناء على ذلك، إحتساب الإختلافات في النمو بين ثلاث مناطق رئيسية هي المنطقة الشمالية، والجنوبية الغربية والوسطى.

النتائج: هناك فروقات ملموسة في النمو بين المناطق استندت إلى السن والجنس ومعامل النمو والمنطقة السكانية. وُجد الفرق الأعلى بين الأطفال والمراهقين في المنطقة الجنوبية الغربية وسكان المنطقتين الأخريين. وقد أثر هذا الفرق في جميع معاملات النمو عند الذكور والإناث على حد سواء.

الاستنتاج: يجب أخذ فروقات النمو المناطقية بعين الإعتبار لدى تقييم النمو عند الأطفال والمراهقين من السعوديين.

منسب كتلة الجسد عند الأطفال والمراهقين السعوديين: مرجع وطني ومقارنة مع البيانات العالمية

مقدمة: نظراً لعدم وجود مرجع مُقنن لمنسب كتلة الجسد عند الأطفال السعوديين، فقد عملنا على تأسيس مُنحنيات لمرجع منسب كتلة الجسد عند الأطفال والمراهقين السعوديين الطبيعين، ومقارنتها بالمعايير العالمية.

المرضى والطرق: قمنا بجمع بيانات من عينة طباقية احتمالية متعددة المراحل من ١٣ منطقة صحية في المملكة العربية السعودية، كجزء من مسح صحي وطني للأطفال والمراهقين السعوديين يهدف إلي تأسيس مراجع للنمو الجسدي الطبيعي. قام فريق مُدرب بزيارة منازل منتخبة، وجرى قياس الوزن والطول/الإرتفاع وتدوين النتائج وفقاً لمعايير منظمة الصحة العالمية وباستخدام نفس المعدات، التي خضعت لمعايرة الفروق بين القرّاء والقراءات.

النتائج: أسفر مسح ١١٨٧٤ منزلاً مؤهلاً عن وجود ٣٥٢٧٥ طفلاً ومراهقاً صحيحاً خضعوا لقياسات بشرية. وتم إنتاج أربعة (٤) مناسب لكتلة الجسد، من زمن الولادة وحتى ٣٦ شهراً ومن ٢ إلى ١٩ سنة للإناث والذكور. كما تم إنتاج المنسب الثالث والخامس والعاشر والخامس والعشرين والخمسين والخامس والسبعين والخامس والثمانين والتسعين والخامس والتسعين والسابع والتسعين ومقارنتها ببيانات منظمة الصحة العالمية ومراكز مكافحة الأمراض.

الاستنتاج: تعكس منحنيات منسب الجسد وتمثل إحصائياً قِيم منسب كتلة الجسد عند الأطفال والمراهقين السعوديين.

الخلاصات العربية

المدونات الطبية السعودية

مرة كل شهرين عن مستشفى الملك فيصل التخصصي ومركز الأبحاث ، ص.ب ٣٣٥٤ ، الرياض ١١٢١١، المملكة العربية السعودية. يتم توزيع المدونات وإعداد الملخصات العربية بالتعاون مع د. زهير القاوي بواسطة موظفي إدارة الخدمات الإدارية بمستشفى الملك فيصل التخصّصي ومركز الأبحاث. جميع المراسلات والاستفسارات وطلبات الاشتراك ترسل إلى المحرر الأول مكتب المطبوعات (ر.إ ٣٦).

سعر الاشتراك ١٠٠ ريال في السنة للأفراد داخل المملكة و٢٠٠ ريال في السنة للأفراد خارج المملكة و٥٠٠ ريال في السنة للمؤسسات. يمكن فتح اشتراك مجاني للأفراد و المؤسسات في الدول النامية.

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هاتف: ٩٦٦-١-٤٦٤٧٢٧٢ تحويلة ٣١٨١٥/٣١٨١٩
فاكس: ٩٦٦-١-٤٦٤٧٢٧٢ تحويلة ٣١٨٧٥
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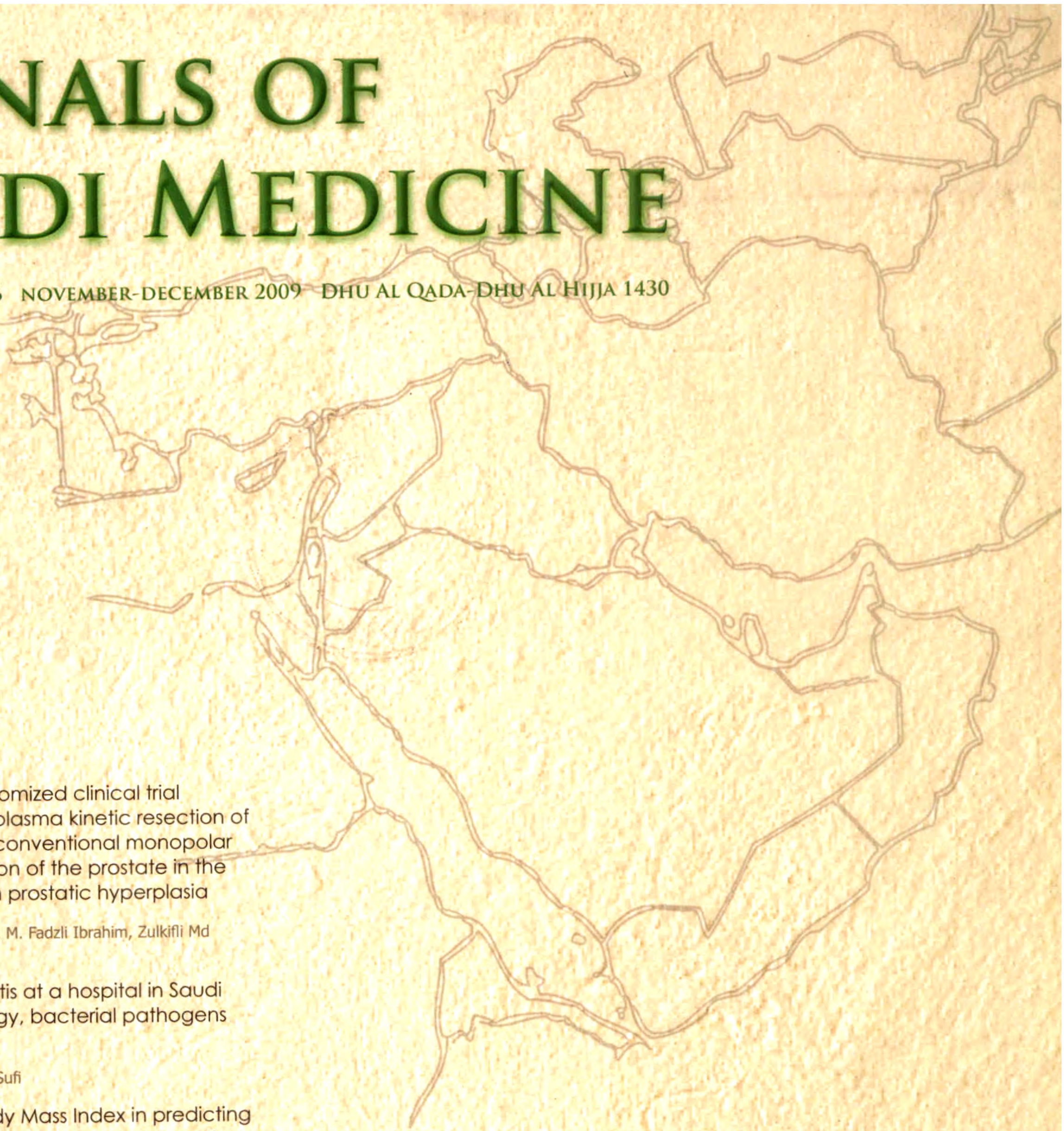

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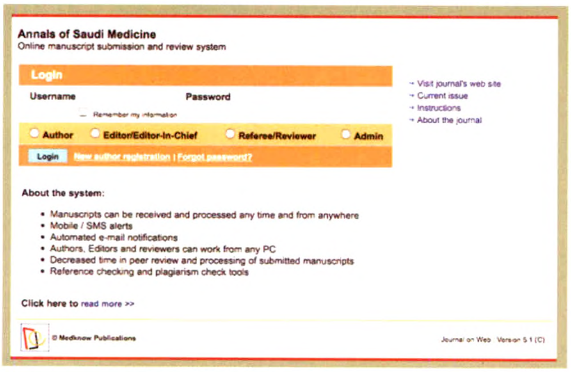
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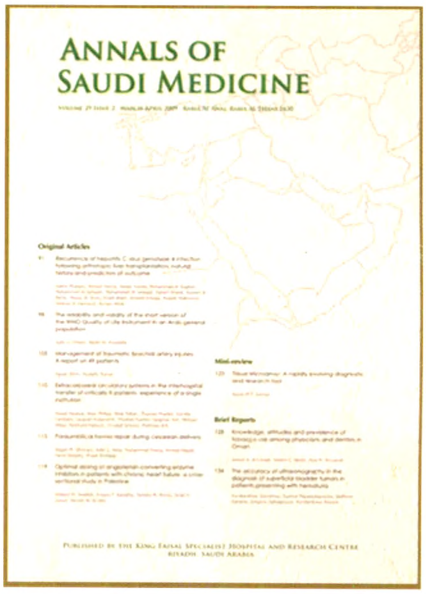
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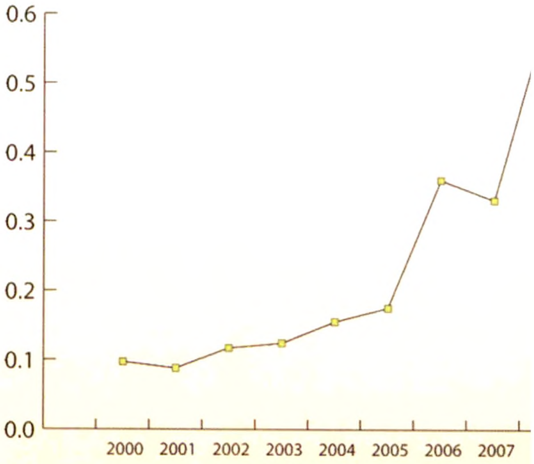

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JANUARY (1)

3rd KFSH&RC Residents' Research Day
20 January 2010 / 05 Safar 1431
Contact No.: 4647272 Ext 31730 (Research Center)

MARCH (6)

2nd International Conference on "Radiation Medicine: Innovative Approaches & Interprofessional Practice"
01-04 March 2010 / 15-18 Rabi Al Awal 1431
Contact No.: 4427879 (Biomedical Physics, Research Center)

1st Middle East Symposium on Diseases of the Esophagus
09-10 March 2010 / 23-24 Rabi Al Awal 1431
Contact No.: 4647272 Ext. 32958 (Surgery)

22nd Saudi Urological Conference
15-18 March 2010 / 29 Rabi I – 02 Rabi II 1431
Contact No. 4647272 Ext. 31830 or 4424302 (Urology)

1st International Conference in Pediatric Emergencies, Injury & Disability Prevention
23-25 March 2010 / 07-09 Rabi Al Thani 1431
Contact No.: 4424425 (Emergency Medicine)

Annual Saudi Colorectal Surgery Forum
27-31 March 2010 / 11-15 Rabi Al Thani 1431
Contact No.: 4427754 (Surgery)

3rd Mini AABB Symposium
30 March – 01 April 2010 / 14-16 Rabi Al Thani 1431
Contact No.: 4424224 (Pathology & Laboratory Medicine)

APRIL (3)

1st Annual Pediatric Nephrology Meeting
06-07 April 2010 / 21-22 Rabi Al Thani 1431
Contact No.: 4427798 (Pediatrics)

Medication Safety: A Mission for All Symposium
13-14 April 2010 / 28-29 Rabi Al Thani 1431
Contact No.: 4427601(Pharmacy Services Division)

International Symposium on New Frontiers in Breast Cancer
27-29 April 2010 / 13-15 Jumada Al Awal 1431
Contact No. 4647272 Ext. 31830 or 4423940 (Oncology Center)

MAY (7)

Conference on Diagnostic & Prognostic Testing in Clinical Biochemistry – A New Age of Disease Biomarkers
04-05 May 2010 / 20-21 Jumada Al Awal 1431
Contact No.: 4427224 (Pathology & Laboratory Medicine)

Oncology Centre Academic & Research Day
05 May 2010 / 21 Jumada Al Awal 1431
Contact No.: 4647272 Ext 38005 Oncology Center

Preventative Genetics: New Initiatives Workshop
11-12 May 2010 / 27-28 Jumada Al Awal 1431
Contact No.: 4424988 (Medical Genetics)

12th Clinical Research Professionals' Course
15-26 May 2010 / 01-12 Jumada Al Thani 1431
Contact No.: 4424987
(Centre for Clinical Studies and Empirical Ethics)

Special Care Dentistry Symposium
18-19 May 2010 / 04-05 Jumada Al Thani 1431
(Workshop on 20 May 2010 / 06 Jumada Al Thani 1431)
Contact No. 4647272 Ext. 31830 or 4427652 (Dentistry)

Ultrasound Guided Regional Anesthesia & Vascular Access Workshop
26-27 May 2010 / 11-12 Jumada Al Thani 1431
Contact No.: 4647272 Ext. 32680 (Anesthesiology)

8th Annual Academic Day
26 May 2010 / 12 Jumada Al Thani 1431
Contact No.: 4423934 (Pediatric Hematology / Oncology)

JUNE (2)

3rd Pediatric Infectious Diseases Seminar
01-02 June 2010 / 18-19 Jumada Al Thani 1431
Contact No.: 4427761 (Pediatrics)

5th LC & LCMS: Concept & Hands-On Training
05-09 June 2010 / 22-26 Jumada Al Thani 1431
Contact No.: 4424987
(Centre for Clinical Studies and Empirical Ethics)

SEPTEMBER (1)

International Symposium on Adult Spine Tumor
28-29 September 2010 / 19-20 Shawwal 1431
(Workshop on 30 September 2010 / 21 Shawwal 1431)
Contact No. 4647272 Ext. 31830 or 4427591 (Orthopedic Surgery)

OCTOBER (8)

8th Pediatric Intensive Review Course
02-07 October Oct 2010 / 23-28 Shawwal 1431
Contact No.: 4427763 (Pediatrics)

Internal Medicine Saudi Board Review Course
07-15 October 2010 / 28 Shawwal – 07 Dhu AlQada1431
Contact No.: 4427495 (Medicine)

2nd Point of Care Testing Workshop "The New Directions in Collaborative POCT Technology Network"
12-13 October 2010 / 04-05 Dhu Al Qada 1431
Contact No.: 4427224 (Pathology & Laboratory Medcine)

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16-27 October 2010 / 08-19 Dhu Al Qada 1431
Contact No.: 4424987
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Adult Congenital Heart Disease Awareness Day
18 October 2010 / 10 Dhu Al Qada 1431
Contact No.: 4647272 Ext. 32452 (King Faisal Heart Institute)

Congenital Heart Disease Symposium
19-20 October 2010 / 11-12 Dhu Al Qada 1431
Contact No. 4647272 Ext. 31830 or 32452
(King Faisal Heart Institute)

2nd International Pain Management Symposium
26-28 October 2010 / 18-20 Dhu Al Qada 1431
Contact No.: 4647272 Ext. 32680 (Anesthesiology)

10th Annual Surgical Research & Residents Day
28 October 2010 / 20 Dhu Al Qada 1431
Contact No.: 4427753 (Surgery)

NOVEMBER-DECEMBER (4)

A New Vision in Medical Nutrition Symposium
30 Nov – 01 Dec 2010 / 24-25 Dhu Al Hijja1431
Contact No. 4647272 Ext. 31830 or 4427206
(Nutrition Services)

7th Annual AIDS Workshop
01 December 2010 / 25 Dhu Al Hijja 1431
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Treatment Modalities for Genetic Diseases: From Diet to Gene Therapy Workshop
07-08 December 2010 / 01-02 Muharram 1432
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6th LC & LCMS: Concept & Hands-On Training
25-29 December 2010 / 19-23 Muharram 1432
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Medknow Publications & Media Pvt. Ltd.,
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Ghatkopar (E), Mumbai-400075, India.

The *Annals of Saudi Medicine* is published bimonthly by King Faisal Specialist Hospital & Research Centre. Arabic abstracts are prepared, in association with Dr. M. Zuheir Al-Kawi, by the staff of the Office Services Department of King Faisal Specialist Hospital & Research Centre.

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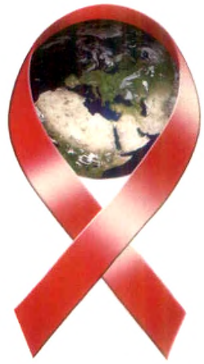

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SUMMARIES

UROLOGICAL SURGERY

A prospective, randomized clinical trial comparing bipolar plasma kinetic resection of the prostate versus conventional monopolar transurethral resection of the prostate in the treatment of benign prostatic hyperplasia

Kong and colleagues randomly assigned 102 patients to either of two procedures for treatment of benign prostatic hyperplasia. Relief of obstructive symptoms and operative time were not different, but the group undergoing the bipolar treatment had a smaller decline in hemoglobin, a lower reduction in serum sodium levels, a shorter cathertization time, and a shorter hospital stay. They concluded that the bipolar treatment has a similar outcome and a lower morbidity than conventional monopolar transurethral resection of the prostate.

INFECTIOUS DISEASE

Infective endocarditis at a hospital in Saudi Arabia: epidemiology, bacterial pathogens and outcome

Al-Tawfiq and Sufi describe 83 cases of endocarditis that occurred at the Dhahran Health Center from January 1995 to December 2008. For 54 patients with definite endocarditis based on Duke criteria, including 39 males and 15 females with a mean (SD) age of 59.7 (18.2) years, native valve endocarditis was observed in 44 (81.5%) and prosthetic valve endocarditis in 10 (18.5%). Most commonly involved were the mitral (n=24; 44.4%) and aortic valves (n=20; 39.2%). The most common organisms were *S aureus* (n=23; 42.6%), *E faecalis* (n=12; 22.2%) and viridans streptococci (n=9; 16.7%). The in-hospital mortality was 29.4%.

DIABETES AND HYPERTENSION

Performance of body mass index in predicting diabetes and hypertension: A study from the Eastern Province of Saudi Arabia

Almajwal and colleagues analyzed data from a screening campaign on 197 681 adults in Saudi Arabia to assess which BMI cutoff values predict the presence of diabetes and hypertension. For cutoff values of 28.50 to 29.50 in men and 30.50 to 31.50 in women, sensitivity and specificity was too low and misclassification too high. Odds ratios for hypertension and/or diabetes increased significantly at BMI values as low as 21-23. They concluded that in the Saudi population, there is no cutoff BMI value that is highly predictive of these chronic diseases.

HEMATOLOGY

Inferior vena caval filters: 5 years of experience in a tertiary care center

In a retrospective study, Saour and colleagues found that 75 of 225 patients with venous thrombosis over a 5-year period had an IVC filter inserted, most frequently for bleeding (62%). Only one patient had a complication related to the infection. Indications were consistent with the current standard of care and complication rates were low.

DIABETES

Renal biopsy in patients with type 2 diabetes mellitus: indications and nature of the lesions

Ghani and colleagues reviewed 31 biopsies performed on type 2 diabetics for clinically suspected non-diabetic renal disease (NDRD). NDRD with underlying diabetic glomerulosclerosis (DGS) was found in 4.2% of biopsies. Of those, crescentic glomeronephritis was present in 21.4%, acute tubulointerstitial nephritis in 14.4% and hypertensive changes in 14.4%. Patients with isolated DGS had greater proteinuria, but did not differ in age, duration of diabetes, gender, presence of hypertension, hematuria, serum creatinine, or glomerular filtration rate.

PULMONARY DISEASE

Clinical characteristics and computed tomography findings in Arab patients diagnosed with pulmonary sarcoidosis

Of 104 patients with pulmonary sarcoidosis, Alhamad and colleagues found that 77% were older than 40 years of age and that females outnumbered males by about 2:1. The most common complaints were dyspnea, cough, and weight loss. Most had impairment in lung function. The most common CT finding was mediastinal lymph node enlargement. Clinical manifestations were similar to those seen in the rest of the world.

A prospective, randomized clinical trial comparing bipolar plasma kinetic resection of the prostate versus conventional monopolar transurethral resection of the prostate in the treatment of benign prostatic hyperplasia

Christopher Ho Chee Kong, M. Fadzli Ibrahim, Zulkifli Md Zainuddin

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Ann Saudi Med 2009; 29(6): 429-432
PMID: 19847078 DOI: 10.4103/0256-4947.57163

BACKGROUND AND OBJECTIVE: For treatment of benign prostatic hyperplasia (BPH), Plasma Kinetic loop Resection of the Prostate (PKRP) is an alternative to conventional monopolar transurethral resection of prostate (TURP). We compared outcomes with the two treatments in a randomized trial.
PATIENTS AND METHODS: Over a one-year period, we randomly assigned patients with an indication for surgery for BPH and who met inclusion criteria to treatment with either PKRP or TURP. We measured prostate volume by transrectal ultrasound, relief of bladder outlet obstruction, operative time, decline in serum sodium and hemoglobin, weight of resected prostatic chips, duration of catheterization and hospital stay. Patients were evaluated one month after discharge for obstructive symptoms. Complications were also recorded.
RESULTS: Of 102 patients enrolled, 51 underwent PKRP and 51 underwent TURP. Relief of obstructive symptoms and mean operative time showed no statistically significant difference. The PKRP group had a smaller decline in hemoglobin than the TURP group (0.6 g/dL vs 1.8 g/dL, *P*=.01), a lower reduction in serum sodium levels (1.03 mmol/L vs 5.01 mmol/L, *P*=.01), a shorter catheterization time (37.2 hours versus 57.7 hours, *P*=.03) and a shorter hospital stay (1.5 days versus 2.6 days, *P*=.02). One patient in the bipolar PKRP group needed recatheterization versus four patients in the TURP group.
CONCLUSION: PKRP reduces morbidity with an outcome similar to conventional monopolar TURP in the treatment of BPH.

Transurethral resection of prostate (TURP) is currently the gold standard for surgical treatment of benign prostatic hyperplasia (BPH) as this procedure results in the best improvement in symptoms and urine flow rate.[1] However, this procedure is not free of complications. Mebust et al reported an 18% morbidity rate after TURP and a metanalysis by the BPH Guideline Panel showed that the morbidity rate associated with TURP ranges from 7% to 43%.[2] This has brought about the emergence of alternative modes of treatment for BPH with the aim of reducing complications, morbidity, hospital stay and cost. plasma kinetic loop resection of the prostate (PKRP) is one such option. It is a relatively new method that has been reported to produce results comparable with conventional TURP.[3] PKRP uses bipolar diathermy as compared with the conventional monopolar diathermy in TURP. We compared the outcome in the relief of bladder outlet obstruction (BOO), complications, operative time and hospital stay, between these two instruments.

PATIENTS AND METHODS

From November 2007 to October 2008, patients with an indication for surgery for BPH were enrolled in a prospective, randomized clinical trial comparing bipolar PKRP versus conventional TURP. The indications for surgery were either moderate to severe Lower Urinary Tract Syndrome that had failed medical treatment, had complications of BOO, or catheter dependency. Exclusion criteria were American Society of Anethesiologists score more than II, use of a pacemaker, suspected or known prostate cancer, concurrent bladder stone and previous bladder neck surgery. Approval was obtained from the Universiti Kebangsaan Malaysia Research and Ethics Committee.

All patients enrolled in the study were given a thorough explanation of both modes of treatment and informed consent was taken prior to randomization. Allocation concealment was done via sequentially numbered, opaque, sealed envelopes. Computerized random-number generator was then used to select an envelope for each patient. A nurse not involved in this study then read the content of the envelope and assigned the appropriate method of surgery. All patients were blinded to the type of treatment method. Preoperatively, BOO was assessed using the International Prostate Symptom Score (IPSS) score, peak flow volume (Qmax) and post-void residual urine volume (PVR) for the severity of the BPH. Blood tests were sent for hemoglobin (Hb) and serum sodium levels.

Both surgeries were performed under spinal anaesthesia by two consultants, both with 5 years experience as consultant urologists. Prostate volumes were measured using transrectal ultrasound. The surgical cutting electrode instruments were of similar design and the surgical technique was also similar in both methods. Storz Fr27 continuous flow resectoscopes with loop electrodes were used in both procedures. Plasma kinetic resection of the prostate was performed using bipolar plasma kinetic tissue management electrosurgical system (Gyrus Medical Ltd, Buck, UK) with the power setting at 240W for vaporization and 60W for coagulation. Conventional TURP was carried out using Pfizer (Valleylab-Monopolar Diathermy) electrosurgical instrument system with the setting at 60W for coagulation and 120W for cutting. In bipolar PKRP, electrical energy is delivered via a bipolar generator. An ionized plasma pocket is created that allows resection and vaporization of the tissue along with haemostasis. Both the active and return electrode are contained within the instrument. Saline solution is used as an electrolytic medium to conduct the electrical energy from the active to the return electrode. In contrast, conventional TURP is performed using monopolar electric current from the electrosurgical unit which flows from the active electrode (the wire loop), through the patient, to an electrosurgical unit grounding pad. Glycine, which is a non-conducting fluid, is used for irrigation.

Operative time was recorded as the time from the introduction of the cystoscope until the insertion of 22F 3-way Foley catheter for normal saline irrigation.

At the end of the surgery, the weight of the prostate chips were measured. Signs and symptoms of transurethral resection (TUR) syndrome were also assessed clinically. Hemoglobin (Hb) and serum sodium levels were reassessed at one hour and 24 hours post-operatively. Bladder irrigation with normal saline was continued until there was no more hematuria. The catheter was then removed within 24 hours of clear urine except in patients who developed complications such as hematuria and clot retention. In those patients, a rigid cystoscope was performed, bleeders diathermised and the catheter was then removed after 24 hours of clear urine. Changes in hemoglobin, hematocrit, serum sodium level, catheterization time, duration of hospital stay and other complications were recorded. Patients were reviewed one month later for evaluation of the effectiveness of the treatment in the relief of BOO as well as to document any complications.

Sample size was calculated a priori with the alpha level set at 0.05, an anticipated effect size (Cohen's *d*) of 0.5 and a desired statistical power level of 0.8. The required sample size per group was 51. A paired *t*-test and Mann-Whitney test were used for the analysis of the variables and categorical data. Differences were considered significant at a *P* value less than .05.

RESULTS

The 102 patients enrolled in the study were randomized into groups of 51 patients each. The median age was 68 years (range, 41-82 years old) (Table 1). The study population included 52 Malays (51.0%), 43 Chinese (42.1%), and 7 Indians (6.9%). The main indication for surgical intervention was failed medical treatment (55%). Pre-operative assessments of the severity of BPH are shown in Table 1. The mean postoperative IPSS score was 6.1 in the PKRP group and 6.5 in the TURP group (*P*=.60). Assessment of mean peak flow volume (Qmax) value at one month postoperation showed a significant improvement to 16.6 mL/s in the PKRP group (*P*=.02 and 17.6 mL/s in the TURP group (*P*=.01). Statistical analysis between the mean difference of peak flow volume (Qmax, pre- and postoperatively) against the type of surgery showed no significant difference (*P*=.29). Mean post-void residual

(PVR) volume improved postoperatively to 21.2 mL in the PKRP group and to 24.3 mL in the TURP group (*P*=.17). Differences in the decline in hemoglobin and serum sodium and in catherization time and hospital stay between the groups were statistically significant (Table 2).

Reassessment one month after surgery showed no significant differences in patient satisfaction in the relief of BOO. The average pre-operative prostate volume was 41.8 mL in the PKRP group and 43.1 mL in the TURP group. The mean chip weight of the resected prostate glands were 24.7 g in the PKRP group and 26.6 g in the TURP group (*P*=.446), meaning that 62.4% and 59.1% of the glands, respectively, were resected (Figure 1).

There were no major complications in either group. No transurethral resection (TUR) syndrome was noticed clinically in any of the patients. Only one patient in the PKRP group needed recatheterization whereas four patients in the TURP group required recatheterization. Of those, two patients failed catheter removal and were discharged with an indwelling catheter. Two of the patients in the TURP group also needed prolonged hospitalization (one patient stayed five days and the other one needed seven days-post operative hospital stay) due to secondary hemorrhage that required blood transfusion.

Table 1. Summary of variables measured.

Variable	PKRP Mean (SD) Pre-op	PKRP Mean (SD) Post-op	Monopolar Mean (SD) Pre-op	Monopolar Mean (SD) Post-op
Age (years)	68.44 (7.33)		68.53 (6.69)	
TRUS (mL)	41.8 (9.80)		43.1 (10.94)	
IPSS	23.3 (4.77)	6.10 (1.47)	23.9 (4.32)	6.50 (1.33)
QOL	4.47 (0.81)	1.98 (0.60)	4.51 (0.76)	1.80 (0.37)
Q max (mL/s)	4.99 (1.48)	17.64 (2.86)	4.60 (1.61)	16.51 (2.53)
PVR (mL)	107 (28.01)	24.21 (5.76)	103 (24.83)	21.37 (6.62)
Hb (g/dL)	12.67 (2.04)	12.10 (1.56)	12.82 (1.16)	12.60 (1.67)

IPSS=International Prostate Scoring System; QOL=quality of life score; Qmax=maximum flow rate; PVR=post-void residual urine volume; TRUS=transrectal ultrasound; SD=standard deviation; Hb=hemoglobin

Table 2. Summary of significant results.

Variable	PKRP Mean(SD)	TURP Mean(SD)	*P*
Hemoglobin decline (g/dl)	0.6 (1.48)	1.8 (1.41)	.01
Serum sodium decline (mmol/l)	1.03 (2.36)	5.01(1.77)	.01
Catheterization time (hours)	37.2 (15.03)	57.7 (17.31)	.03
Hospital stay (days)	1.5 (0.88)	2.6 (0.92)	.02

SD=standard deviation; PKRP=plama kinetic resection of prostate; TURP=transurethral resection of prostate

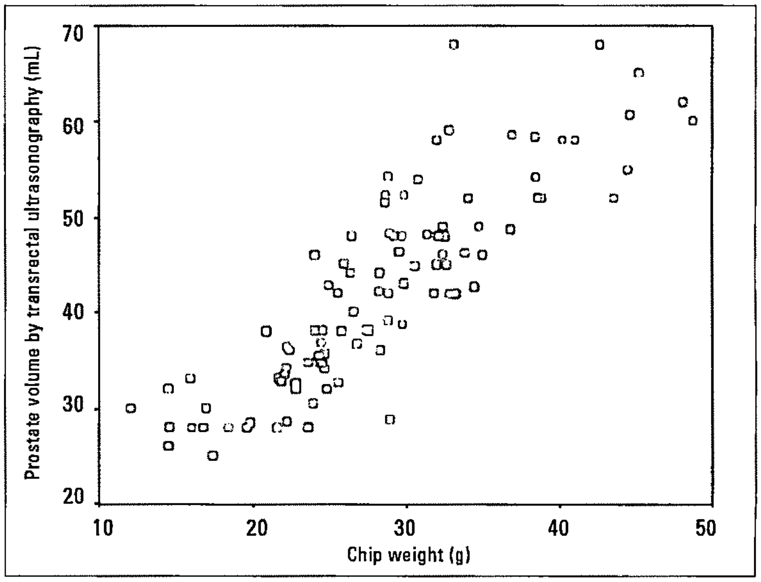

Figure 1. Correlation between transurethral ultrasound prostate volume (mL) and prostatic chip weight resected (g).

DISCUSSION

Standard transurethral resection uses basic electrosurgical principles to achieve effective and rapid removal of prostate tissue. Recently, plasmakinetic electrovaporization uses these principles to combine vaporization and resection in a simultaneous action that achieves the desired effects of the standard conventional TURP.[1] There have been a number of studies reporting improvements in objective parameters compared to conventional TURP.[1-9] In the present trial, the main objective of evaluating the outcome in relief of BOO between the two groups did not show a statistically significant difference (parameters measured were IPSS score, Qmax and PVR different pre- and postoperatively). This finding was also observed in a previous series.[4,6] This may indicate that the plasmakinetic method has comparable effect in relief of bladder obstruction symptoms (equivalent effect to standard conventional group).

The mortality associated with TURP is very low (less than 0.25%). However, the procedure has complications, such as blood loss, that need blood transfusion (up to 8%) and transurethral resection (TUR) syndrome (up to 2%).[6] The sharp cutting action using plasmakinetic electrovaporization and resection using a loop electrode (as in the Gyrus system) should prevent these complications, improving homeostasis during the procedure and reducing the risk of hyponatremia (normal saline instead of glycine was used as the irrigation fluid).[6,10-13] The bipolar electrosurgical equipment simultaneously vaporizes tissue during resection, which controls bleeding as it effectively and accurately seals all bleeding points.[8,10,14,15] The plasmakinetic system, however, uses a smaller loop compared with the conventional TURP, which requires more strokes for every unit volume of prostate resected.[9,16-18] This explains the insignificant operative time difference between the two groups despite the advantage of better hemostasis.[9,17,18]

The systemic absorption of glycine contributes to TUR syndrome.[11,12] The risk increases from 0.7% to 2% if the resection time is longer than 90 minutes and for a larger prostate (>45 g).[11,12] Using the plasmakinetic system reduces the risk as the irrigation solution used is normal saline. In our series, TUR syndrome was not observed in both groups. Even though the serum sodium drop in conventional monopolar group showed statistical significance (*P* value <.05), it was only detected biochemically and was not severe enough to cause clinical manifestation of TUR syndrome.

Blood loss is the most frequent postoperative complication of TURP. In our cohort, the mean decrease in hemoglobin level at 24 hours after surgery was lower in the plasmakinetic bipolar group and this was statistically significant (*P*<.05). There was no major bleedin episode in plasmakinetic bipolar group, while in th conventional monopolar group two patients develope secondary hemorrhage that needed blood transfusion This effect of better homeostasis was also seen in man previous studies[4,6] except that some did not show statistical significance change.

The patients treated by the plasmakinetic bipola method had their catheter removed at mean of 37. hours, which was earlier compared to the conventiona monopolar group (mean 57.7 hours). This advantag was observed mostly due to a better hemostatic effec exerted by the plasmakinetic method. This was obviously followed by a shorter post-operative hospital sta in the plasmakinetic bipolar group (mean 1.5 days compared to the conventional monopolar group (mea 2.6 days) thus translating into a reduction of cost (earlier discharge from hospital).

In conclusion, PKRP is comparable to TURP i terms of efficacy in the relief of BOO. It has the further advantage of better hemostasis as proven by les blood loss, no significant reduction of serum sodium less catheterization time and a shorter hospital stay. I may also enable prostate resection as a day case in selected cases. These data are promising, but a longer follow up and larger series are needed to compare the lat complications such as urethral stricture, bladder nec stenosis and retrograde ejaculation, before the bipola PKRP method becomes universally accepted for managing BPH.

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original article

Infective endocarditis at a hospital in Saudi Arabia: epidemiology, bacterial pathogens and outcome

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Ann Saudi Med 2009; 29(6): 433-436
PMID: 19847079 DOI: 10.4103/0256-4947.57164

BACKGROUND AND OBJECTIVE: Data on infective endocarditis prevalence, epidemiology and etiology from Saudi Arabia and the Gulf region are sparse. We undertook this study to describe the pattern and the causative agents of endocarditis at a hospital in Saudi Arabia.
METHODS: We conducted a retrospective analysis of all reported endocarditis cases at the Dhahran Health Center from January 1995 to December 2008.
RESULTS: Of the 83 cases of endocarditis, 54 (65%) were definite endocarditis and the remaining 29 (35%) were possible endocarditis based on the Duke criteria. Patients with definite endocarditis included 39 males and 15 females (ratio of 2.6:1) with a mean age (SD) of 59.7 (18.2) years. Of the definite endocarditis cases, native valve endocarditis occurred in 44 (81.5%) cases of and prosthetic valve endocarditis was observed in 10 (18.5%). The most commonly involved valves were mitral (n=24; 44.4%) and aortic (n=20; 39.2%). The most common organisms were *S aureus* (n=23; 42.6%), *Enterococcus faecalis* (n=12; 22.2%) and viridans streptococci (n=9; 16.7%). Surgical intervention was required in 17 (31.4%) cases and the in-hospital mortality rate was 29.4% (n=15). Of all the patients, 3 (5.5%) had embolic stroke as a complication.
CONCLUSION: Native valve endocarditis is the predominant type of endocarditis. The patients were older adults and the most common organisms were *S aureus, E faecalis* and viridans streptococci.

Infective endocarditis (IE) is associated with high morbidity and mortality rates. The current reported in-hospital mortality rate for patients with IE is 15% to 20% with a 1-year mortality rate approaching 40%.[1] Over the past 20 years, significant changes in the demographic characteristics of IE were reported, including a shift in the age group and a change in the causative organisms.[1,2] A single report suggested that *S aureus* was the more common etiological agent of IE in children.[3]

Data on IE prevalence, epidemiology and etiology from Saudi Arabia and the Gulf region are lacking. Apart from case reports of endocarditis, there is only one study addressing the epidemiology of endocarditis in Saudi Arabia.[4] Hence, we undertook this study to describe the clinical, microbiological and echocardiographic characteristics as well as the complications of endocarditis in a Saudi Arabian hospital.

METHODS

This was a retrospective analysis of cases of endocarditis from January 1995 to December 2008 at Saudi Aramco Medical Services Organization (SAMSO). SAMSO provides medical care for Saudi Aramco employees and their dependents: spouses, children and parents (currently, approximately 370 000 individuals are eligible for medical care). The main hospital, Dhahran Health Center (DHC) has a capacity of 380 beds. Admissions to the hospital cover a whole range of patients and include general ward admissions, intensive care and patients receiving chemotherapy for hematological and solid organ malignancy. There are five critical care units including an open heart surgery unit. Transesophageal echocardiography is available. At DHC, medical therapy of patients with IE followed the guidelines of the American Heart Association.[5]

IE cases were retrieved from the computerized database of the health information unit. The case definitions of endocarditis were based on the modified Duke criteria and cases were classified as definite or possible cases accordingly.[6] We collected the following data: age, gender, predisposing factors, the causative organism, the presence or absence of vegetations on the echocardiogram, the involved cardiac valves, surgical intervention, the indication for surgery, and the 30-day mortality. The data was processed using Statistical Package for the Social Sciences SPSS (10.0). The study was approved by the public relations department in accordance with Saudi Aramco Medical Services Organization policy and procedure (approval number 9-1796).

RESULTS

A total of 83 cases of endocarditis were identified and 54 (66%) cases were classified as definite endocarditis. The remaining 29 (35%) were possible endocarditis (based on the Duke criteria) and thus were excluded from further analysis. For patients with definite endocarditis, there were 39 males and 15 females (ratio of 2.6:1) with a mean age (SD) of 59.7(18.2) years. The overall incidence of endocarditis was 15.6 per 100 000 discharges during the study period.

Native valve endocarditis occurred in 44 (81.5%) and prosthetic valve endocarditis was observed in 10 (18.5%). Four patients (7.4%) were thought to have healthcare-associated endocarditis. The most commonly involved valves were the mitral (n=24; 44.4%) and aortic valves (n=20; 39.2%) (Table 1). The most common organisms were *S aureus* (n=23; 42.6%), *Enterococcus faecalis* (n=12; 22.2%) and viridans streptococci (n=9; 16.7%) (Table 2). Transthoracic echocardiography (TTE) showed vegetation in 37 (72.5%) and TEE showed vegetation in all the patients who had TEE (n=32) (Table 3). Moreover, TEE detected vegetation in 14 (27.7%) patients whom TTE was negative or questionable (Table 3).

Surgical intervention was required in 17 (33.3%). Of all cases who had surgical intervention, 9 (53%) were due to acute valvular rupture or perforation, 5 (29.4%) due to large vegetations (>10 mm) and two (11.6%) had perivalvular abscess. The in-hospital mortality rate was 29.4% (n=15). The highest mortality rate among patients with *S aureus* endocarditis was 43.7% (7/16 cases) compared to 26.3% (9/35 cases) in other cases (*P*=.221). Of all the patients, 3 (5.5%) had embolic stroke as a complication.

Table 1. Involved cardiac valves based on the echo cadiographic findings.

Involved value	Number	%
Prosthetic valve endocarditis	10	18.5
Aortic valve bioprosthesis	3	5.6
Aortic valve bioprosthesis, mitral valve	1	1.9
Aortic mechanical	1	1.9
Tricuspid	1	1.9
Mitral valve bioprosthesis	4	7.4
Native valve endocarditis	44	81.5
Aortic valve, mitral valve	3	5.6
Tricuspid valve	4	7.4
Aortic	17	31.5
Mitral valve	20	37.0
Total	**54**	**100.0**

Table 2. Causative organisms of endocarditis.

Blood culture	Number	%
Gram negative bacteria	5	9.3
Brucella	1	1.9
Enterobacter aerogenes	1	1.9
ESBL-producing *klebsiella*	1	1.9
Pseudomonas aeruginosa	2	3.7
Gram positive bacteria	49	90.7
Staphylococcus aureus	21	38.9
MRSA	2	3.7
Coagulase-negative *staphylococcus*	4	7.4
Viridans streptococci	9	16.7
Enterococcus faecalis	12	22.2
Beta-hemolytic *streptococcus*	1	1.9
Total	**54**	**100.0**

ESBL: extended-spectrum beta-lactamase, MRSA: methicillin-resistant *S aureus*

Table 3. Findings of transthoracic echocardiography (TTE) and transoesophageal echocardiography (TEE) in patients with definite infective endocarditis.

		TEE		
		Positive	**Not done**	**Total**
TTE	Positive	18	19	37
	Negative	11	0	11
	Could not be excluded	3	0	3
Total		**32**	**19**	**51**

DISCUSSION

The epidemiology of IE has shown some changes in the last 30 years.[7] These changes have included the involvement of older age groups and an increased incidence of *S aureus* and gram-negative bacilli. The overall incidence of endocarditis was 15.6 per 100 000 discharges during the study period. Similarly, the incidence rate was 14.6 cases per 100 000 hospital admissions from National Guard Hospital in Riyadh.[4] Thus based on these two studies, the rate of definite endocarditis in Saudi Arabia is estimated to be about 15 cases per 100 000 admissions/discharges.

The mean age of patients with endocarditis was between 28 and 32 years in studies from Saudi Arabia, Kuwait, India and Tunisia.[4,8-10] In contrast, the mean age of the patients in the current study was 58.5 years. This finding is in agreement with recent reports from the United States and Europe. In those studies, 50% or more of endocarditis cases occurred in patients over the age of 60 years, and the median age was 67 years.[11-13] The possible explanations for such a shift are the increasing number of elderly people in the general population and the reduction in the incidence of rheumatic heart disease. The former is particularly true in our hospital with increasing number of geriatric patients.

The most commonly involved valves were the mitral and aortic. This finding is similar to an earlier study from Saudi Arabia where the mitral valve alone was involved in 45.6% and aortic valve in 21.3%.[4] Similarly, isolated aortic and mitral valve infections occurred in 39% and 21%, respectively.[14] Transesophageal echocardiography (TEE) detected vegetation in 27.7% patients whom TEE was negative or questionable. TEE demonstrates greater sensitivity compared to TTE in the detection of vegetation in two studies (100% versus 63% and 94% versus 44%, respectively).[15,16]

We observed that 42.6% of IE cases were due to *S aureus*. Similarly in a study from Saudi Arabia, *S aureus* accounted for 33% of all the cases.[4] The International Collaboration on Endocarditis-Merged Database (ICE-MD) also showed that of all patients with native valve endocarditis, 34% had *S aureus* infection.[17] A similar finding was reported by other investigators and *S aureus* accounted for 50% of endocarditis.[18] However, this finding is in sharp contrast to a study from Kuwait in 1985-1988 where *Streptococcus viridans* was the commonest infective organism.[10] Another study from Lebanon showed that 51% of endocarditis cases were due to *Streptococcus* spp.[19] This difference is related to the time of the study since the current study was done at a later time period.

In a study from National Guard Hospital in Riyadh, methicillin-resistant *S aureus* (MRSA) accounted for 4% of the endocarditis cases.[4] Similarly, we observed that MRSA endocarditis occurred in 3.7% of all cases. This finding is much lower than those reported in a study from the USA where MRSA endocarditis was seen in 14.8% of patients[17] and from Lebanon where MRSA endocarditis occurred in 7% of all cases.[19] The difference may be related to the lower rate of MRSA in our hospital where it constituted 6% of all *S aureus* isolates.[20] Viridans streptococci constituted 16.7% of the cases and we reported previously a case of endocarditis due to *Granulicatella elegans*.[21]

Our results showed that 33.3% of the cases of IE have required surgical intervention. The indications for surgery were acute valvular rupture or perforation, the presence of large vegetations, and perivalvular abscess, according to the published guidelines.[22] The surgical rate was lower than the 44.7% rate reported from another study from Saudi[4] and a 50% rate from Tunisia.[9] In the International Collaboration on Endocarditis–Prospective Cohort Study, surgical therapy was required in 48.2%.[13] The high rate of surgical interventions indicates that the threshold for early surgical treatment is lower than before.[13] It is shown that early surgery may be critical in improving survival in patients with definite IE.[23-25]

S aureus endocarditis carries a high mortality rate. In the current study, the mortality rate of *S aureus* endocarditis was 29.4%, which was not statistically different than other IE cases. In contrast, in a large study of *S aureus* endocarditis, patients with *S aureus* were more likely to die (20% vs. 12%) than other patients.[18] In the International Collaboration on Endocarditis–Prospective Cohort Study, in-hospital mortality was 17.7%.[13] In another study, *S aureus* IE was associated with a higher 1-year mortality rate (43.9% vs. 32.5%;

P=.04).[1] Other studies showed a high mortality rate of *S aureus* endocarditis of at least 40%.[26-28] However, most recent studies still show a high mortality rate, approaching 34%.[29]

There are a few limitations of the current study, as it is retrospective and uncontrolled in design. Second, it involved patients from one institute and may have referral bias. Third, the number of patients is relatively low in comparison to international registries, but is similar to single institution reports. The study shows that developing a national registry for endocarditis throughout Saudi Arabia is an ambition and would be of particular help to health care.

In conclusion, IE remains a serious disease with high morbidity and mortality rates. In addition, IE has shifted to a disease in older adults with a high rate of *S aureus* infections. Geographic differences in the presentation, microbial etiology, treatment, and outcome of patients with IE need to be taken into consideration.[13]

Acknowledgment

The authors acknowledge the use of Saudi Aramco Medical Services Organization (SAMSO) facilities for the research data utilized in this manuscript. Opinions expressed in this article are those of the authors and not necessarily of SAMSO.

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original article

Performance of Body Mass Index in predicting diabetes and hypertension: A study from the Eastern Province of Saudi Arabia

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Ann Saudi Med 2009; 29(6): 437-445
PMID: 19847080 DOI: 10.4103/0256-4947.57165

BACKGROUND AND OBJECTIVES: Body mass index (BMI) is the most widely used measure to define obesity and predict its complications, such as diabetes and hypertension, but its accuracy and usefulness in Saudi subjects is unknown. This study aimed to assess the validity of standard BMI cut-point values in the Saudi population.
SUBJECTS AND METHODS: 197 681 adults participated in a cross-sectional study to detect diabetes and hypertension in the Saudi Eastern province in 2004/2005, with blood pressure, fasting blood sugar, height and weight measurements taken. Sensitivities, specificities, areas under the curves, predictive values, likelihood ratios, false positive, false negatives and total misclassification ratios were calculated for various BMI values determined from receiver operating characteristic (ROC) curves. The significance of the association between risk factors and BMI was assessed using regression analysis.
RESULTS: For the definition of overweight, ROC curve analysis suggested optimal BMI cut-offs of 28.50 to 29.50 in men and 30.50 to 31.50 in women, but the levels of sensitivity and specificity were too low to be of clinical value and the overall misclassification was unacceptably high across all the selected BMI values (>0.80). The relationship between BMI and the presence of diabetes and/or hypertension was not improved when a BMI of 25 was used. Using regression analyses, the odds ratios for hypertension and/or diabetes increased significantly from BMI values as low as 21-23 with no improvement in the diagnostic performance of BMI at these cutoffs.
CONCLUSION: In Saudi population, there is an increased risk of diabetes and hypertension relative to BMI, starting at a BMI as low as 21 but overall there is no cutoff BMI level with high predictive value for the development of these chronic diseases, including the WHO definition of obesity at BMI of 30.

Body mass index (BMI) is widely used as a method to classify underweight, overweight and obesity. Around three quarters of Saudi dietitians use this tool as outcome measure to assess the success in weight loss.[1] BMI is defined as the weight in kilograms divided by the square of the height in meters (kg/m^2). In 1997, the World Health Organization (WHO) proposed cut-off points for classifying overweight and obesity.[2,3] Overweight is classified as BMI ≥25.0 and obesity is classified as BMI ≥30.0. These cutoffs have been identified on the basis of the association between BMI and chronic diseases and mortality.[2,4] Since these criteria were derived from European populations their appropriateness for Non-European populations including the Saudi population, is unclear, and the recent WHO monograph on obesity acknowledged the 'need for different standards that are "culturally specific".[2]

It has been demonstrated that Asians have a higher percentage of body fat than Caucasians at the same BMI cut-off levels and the health risks associated with obesity occur at a lower BMI cut-off level than Caucasians.[5-12] There have been a few attempts to investigate the applicability of the WHO BMI cut-offs in Asian and Pacific populations.[12-18] In 2000, the Regional Office for the Western Pacific Region of WHO with the International Association for the Study of Obesity

(IASO) and the International Obesity Task Force (IOTF) defined overweight in Asians as a BMI >23.0 and obesity as a BMI >25.0.[13] In 2004, WHO did not propose a clear BMI cut-off for all Asians, but they indicated that the cut-off points for observed risk varies between BMI of 22.0 to 25.0 in different Asian populations and these values varies between BMI 26.0 to 31.0 for the high risk cut-off.

Even though BMI has been used extensively in research and clinical practice, there are only a few studies examining its diagnostic accuracy and no study has examined this in a large, non-Caucasian adult population. Therefore, the present study aimed to assess the ability of BMI to diagnose obesity relative to metabolic risk factors and to determine the optimal BMI cut-off points that could be used to classify obesity in the Saudi population.

SUBJECTS AND METHODS

This study used data from a large survey conducted in the Eastern Province of Saudi Arabia in 2004 and 2005. The aim of the survey was the early detection of diabetes and hypertension and a detailed description of the study design and data collection procedures has been published elsewhere.[19] Briefly, all Saudi residents in the Eastern Province aged 30 years and older were invited to participate in the survey. Pregnant women and non-Saudi people were excluded from the survey. For recruitment, a media campaign was organized in each sector using written material and audiovisual media. In addition, posters were put up on billboards along the streets and public places in the Eastern Province. The estimated target population of Saudi residents in the Eastern province aged ≥30 years was 650 000 individuals.[20] A total of 197 681 Saudis responded to the campaign's invitation (30.4%) and 195 851 of them had assessments of height and weight, and presence of diabetes and/or hypertension and were included in the analysis of the present project. The survey through this convenience sample was conducted through more than 300 examination posts run by trained nurses and technicians distributed in the Eastern Province of Saudi Arabia, including all Primary Health Care Centers (PHCCs), governmental hospitals, and several private health places, and other venues, in addition to mobile teams who visited the target population in places of work that had more than 30 employees.

Weight was measured to the nearest 0.5 kg using standardized beam weight scales (Detecto scale, Cardinal Scale Mfg Co., USA) and recorded to the lowest unit without footwear and with only light clothes on. Height was measured to the nearest centimeter with the subjects barefoot and standing with the feet together, ensuring the nape, back, calves and with the ankles pressed against the measuring tape, which is part of weighing scale. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2), and standard WHO cut-off values of a BMI ≥25.0 as overweight and a BMI ≥30.0 as obesity were used to define the prevalence. Blood pressure was measured two times while the subject was at rest in a sitting position. The average of the two measurements was accepted if the difference between the values was less than 5 mm Hg. Measurement was taken using standardized mercury sphygmomanometers (Diplomat Presameter 660-360 manufactured by Riester GMBH, Germany) with an appropriate cuff inflated to a pressure approximately 30 mm Hg greater than systolic and with the subject's arm at the level of the heart. The screening test for hypertension was considered positive if the systolic and diastolic blood pressure was ≥140 and/or ≥90 mm Hg, respectively.[21] The diagnosis of hypertension was made if positive screening was confirmed on a subsequent day, or if there was a history of previous diagnosis, irrespective of the blood pressure reading. Participants who did not come for the confirmatory test were diagnosed as having hypertension if screening test of systolic and diastolic blood pressure was ≥180 and /or ≥110 mmHg, respectively. These relatively high values were chosen to avoid over diagnosing hypertension in participants who might be in rush or anxious from the results of the evaluation.

Whole blood glucose concentration was measured for all participants using uniform portable glucometer machines with a Medisafe Reader (Terumo Co., Tokyo, Japan), based on reflectance photometry, where the glucose was catalytically oxidized by the glucose oxidase and peroxides enzymes with a color change reaction. A screening test was considered to be positive for hyperglycemia if Capillary Fasting Blood Glucose (CFBG) was ≥100 mg/dL (≥5.6 mmol/L) after at least 8 hours of fasting or the Capillary Random Blood Glucose (CRBG) was ≥140 mg/dL (≥7.8 mmol/L) taken without consideration of the time of the last meal.[22] A CFBG of 100-125 mg/dl (5.6-6.9 mmol/l) and a CRBG of 140-199 mg/dl (7.8-11 mmol/l) were considered to be consistent with impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), respectively. Initial screening test was considered to be consistent with the diagnosis of diabetes if the CFBG was ≥126 mg/dl (≥7.0 mmol/l) or the CRBG was ≥200 mg/dl (≥11.0 mmol/l). Diabetes mellitus was diagnosed either by a positive history of diabetes or through the screening test. All subjects who had been screened positive for hyperglycemia without a history of diabetes were asked to come in fasting for ≥8 hours, on the following day, at the central laboratory, for confirmation of the results by venous blood testing through the measurement of fasting plasma glucose (FPG). Confirmatory FPG was considered to be diagnostic for diabetes if it was ≥126 mg/dL (≥7.0 mmol/L). Participants who did not come for the confirmatory test were diagnosed as having diabetes if screening test of CFBG was ≥200 mg/dl (11.0 mmol/l) or CRBG was ≥270 mg/dl (15.0 mmol/l).

Data were analyzed with SPSS software (version 17.0; SPSS Inc., Chicago, IL). All results are presented as mean (SD) or percentage, where applicable. Data analysis was performed in men and women separately. BMI was stratified in unit of 0.5 for both men and women. A BMI <19.9 was considered as the reference. Logistic regression analysis was used to examine the independent relationship between the stratified BMI and the odds ratio of having diabetes, hypertension, both diabetes and hypertension and either diabetes or hypertension. *P* value<.001 was considered to be significant.

The optimal sensitivity and specificity using different BMI cut-off values to predict the presence of diabetes and/or hypertension were examined by receiver operating characteristic curve (ROC) analysis. A greater area under the curve (AUC) indicates better predictive capability. An AUC=0.5 indicates that the test performs no better than chance, and an AUC=1.0 indicates perfect discrimination. An ideal test is one that reaches the upper left corner of the graph (100% true positives and no false positives). To determine the optimal BMI cut-off points, we computed and searched for the shortest distance between any point on the curve and the top left corner on the y-axis. Distance was estimated at each one-half unit of BMI according to the equation:[23,24]

$$\text{Distance in ROC curve} = \sqrt{(1\text{-sensitivity})^2 + (1\text{-specificity})^2}$$

Additional criteria were also used to select cut-offs, including the greater sum of sensitivity and specificity, the smallest misclassification rate, and the significant associations between BMI and risk factors based on the logistic regression. Diagnostic performance of BMI in predicting diabetes and hypertension was assessed by calculating AUC, sensitivity, specificity, predictive values (Positive Predictive Values and Negative Predictive Values), likelihood ratios (LR+ and LR−), false positive (FP), false negative (FN) and the total misclassification rate.

RESULTS

A total of 195 851 participants (99 946 men and 95 905 women) were included in the analysis. Table 1 shows study population characteristics. The overall mean (SD) BMI of participants was 29.69 (6.00). The mean weight and height for men were 80.45 (15.94) kg and 1.67 (0.07) m and for women were 73.29 (16.1) kg and 1.54 (0.07) m, respectively. The overall prevalence of obesity (BMI≥30), overweight (BMI 25-29.9), diabetes and hypertension were 43.8, 35.1, 17.2 and 15.6%, respectively. Results of the initial screening test for participants with no previous diagnosis of diabetes or hypertension showed that 10.9% of participants had IFG, IGT or diabetes and 9% had hypertension. Analysis also showed that 59.3% of participants with diabetes and 46% of participants with hypertension had another confirmatory test. This means 4.4% and 4.9% of the total sample did not have the confirmatory test for the diagnosis of diabetes and hypertension. However, >70% of participants who did not come for the confirmatory test for diabetes had IFG or IGT. For hypertension, 53.0 % of participants had diastolic blood pressure ranged from 140 to 150 mmHg and 77.3% of participants had diastolic blood pressure ranged from 90 to 100 mmHg.

Table 2 displays details of the diagnostic performance of BMI in detecting diabetes and/or hypertension using optimal BMI cut-off values based on the shortest distance in ROC curve. Values ranged from 28.50 to 29.50 in men and from 30.50 to 31.50 in women. The AUC ranged from 0.566 to 0.625 in men and from 0.618 to 0.645 in women (Figure 1). These values were statistically significantly higher than that would be expected by chance alone (*P*<.001).

The corresponding sensitivities and specificities in men ranged from 0.55 to 0.59 and 0.54 to 0.62, respec-

Table 1. Population characteristics (n=195 851).

	Men	Women	Both genders
Weight (kg)	80.45 (15.94)	73.29 (16.1)	76.95 (16.43)
Height (m)	1.67 (0.07)	1.54 (0.07)	1.61 (0.10)
BMI (kg/m²)	28.67 (5.26)	30.75 (6.51)	29.69 (6.00)
Obese (%)	36.1	51.8	43.8
Overweight (%)	40.3	29.7	35.1
Diabetes (%)	15.9	18.6	17.2
Hypertension (%)	13.1	18.1	15.6

Table 2. Diagnostic performance of BMI in detecting diabetes and/or hypertension using optimal BMI cut-off values based on the shortest distance in ROC curves in Saudi adults, Eastern province, 2004, (n=195851).

Risk factors	Gender	n	AUC (95% CI)	Cut-offs kg/m²	Sensitivity	Specificity	PPV	NPV	LR +	LR –	FP rate	FN rate	Misclassification rate
Diabetes	Men	99946	0.566 (0.561-0.571)	28.50	0.55	0.54	0.19	0.87	1.21	0.82	0.46	0.45	0.91
	Women	95905	0.618 (0.614-0.622)	31.50	0.58	0.61	0.25	0.86	1.48	0.69	0.39	0.42	0.81
Hypertension	Men	99946	0.6 25 (0.62-0.63)	29.00	0.59	0.58	0.18	0.91	1.42	0.70	0.42	0.41	0.83
	Women	95905	0.645 (0.641-0.650)	31.50	0.60	0.62	0.25	0.87	1.55	0.66	0.39	0.41	0.80
Diabetes or Hypertension	Men	99946	0.594 (0.590-0.598)	28.50	0.58	0.56	0.13	0.92	1.30	0.76	0.44	0.42	0.86
	Women	95905	0.640 (0.636-0.643)	30.50	0.63	0.58	0.17	0.92	1.47	0.65	0.43	0.37	0.80
Diabetes and Hypertension	Men	99946	0.618 (0.611-0.625)	29.50	0.55	0.62	0.08	0.96	1.44	0.73	0.38	0.45	0.83
	Women	95905	0.643 (0.637-0.649)	31.50	0.61	0.59	0.12	0.94	1.55	0.66	0.41	0.39	0.80

AUC: area under the curve; PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio; LR-: negative likelihood ratio; FP rate: false positive rate; FN rate: false negative rate

tively, and in women they ranged from 0.58 to 0.63 and 0.58 to 0.62, respectively. LRs were close to 1.0 in both men and women. The positive likelihood ratio (LR+) ranged from 1.21 to 1.55 and the negative likelihood ratio (LR–) ranged from 0.66 to 0.82. The PPV were small, ranging from 0.08 to 0.25; NPV were high, ranging from 0.87 to 0.96. FP and FN rates were close to each other and ranged from 0.38 to 0.46 and from 0.37 to 0.45, respectively. The overall misclassification was unacceptably high across all the selected BMI values (>.80). These cut-offs were selected based on the shortest distance in the ROC curves. However, when other criteria applied, including the greater sum of sensitivity and specificity, and the smallest misclassification rate, the results were very similar (data not shown).

Table 3 shows the odds ratios of the association between diabetes and hypertension and BMI in men and women. A significant positive association was observed with BMI values starting at 21 to 23 and increasing progressively with higher BMI values for both genders. Table 4 displays the predictive value of BMI in detecting diabetes and/or hypertension using BMI cut-off values based on the lowest significant association between BMI and the risk factors from the logistic regression analysis. The diagnostic performance of BMI was also assessed using a BMI of 25 (the value recommended by WHO to identify overweight), but the results showed poor performance (data not shown).

DISCUSSION

This is the first population-based study to assess the ability of BMI to diagnose obesity and to determine the optimal BMI cut-off points for the Saudi population based on the prevalence of diabetes and hypertension. BMI has been shown to be associated with cardiovascular diseases such as diabetes and hypertension in Caucasians.[25-27] These relationships, which have been used in many studies to assess the accuracy of BMI in diagnosing obesity, have also been demonstrated in Middle Eastern people, including Saudis.[28-30] The use of a reliable tool with optimal cut-off points for obesity diagnosis is very important to establish consequent public health policies, treatment protocols and to determine the correct prevalence of obesity for each population.

ROC curve analysis, using the endpoints of presence of diabetes or hypertension, showed that the optimal BMI cut-off points for overweight ranged from 28.50 to 29.50 for men and from 30.50 to 31.50 for women depending on the risk factor being studied. These values are higher than the suggested values by WHO, particularly in women. One possible reason for the high value for women is the short stature in this group with a mean

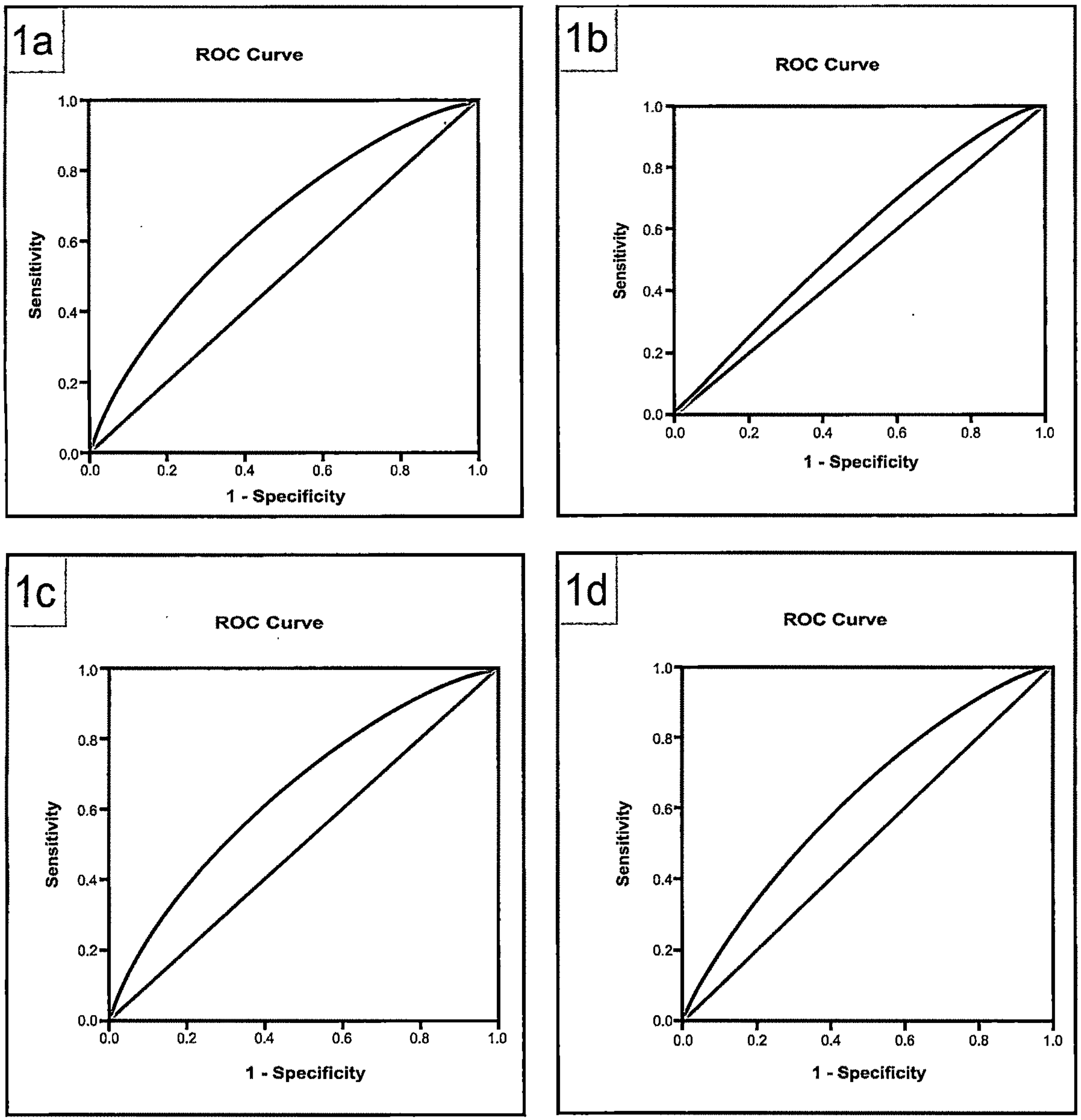

Figure 1. ROC curve showing the performance of BMI in predicting diabetes and hypertension (1a: diabetes in women, AUC=0.618 (95% CI 0.614 to 0.622); 1b: diabetes in men, AUC=0.566 (95% CI 0.561 to 0.571); 1c: hypertension in women, AUC=0.645 (95% CI 0.641 to 0.650); 1d: hypertension in men, AUC=0.625 (95% CI 0.620 to 0.630).

height of 1.54 m. Lara-Esqueda et al[31] conducted a large cross-sectional study (n=119, 975) to assess the ability of the BMI to predict obesity-associated morbidity in Mexican participants with normal or short stature. The results showed that the BMI value with the best diagnostic proficiency ranged from 27 to 29 in normal stature women and from 28 to 29 in short stature women. The authors concluded that the proficiency of BMI as a diagnostic test is poor in short stature participants. However, lowering the BMI threshold did not improve the ability of BMI to predict diabetes and hypertension in that study and neither did it in our study as well.

The overall performance of the ROC curve can be quantified by estimating the AUC which ranged from 0.57 to 0.65 (Table 4). An area of 1.0 is perfect and an area <0.5 is considered non-informative. Our results indicated that the ROC analysis was close to a non-informative test (Figure 1). To avoid a misleading conclusion, several other diagnostic characteristics of BMI as a tool for obesity diagnosis were calculated.

Table 3. Risk of diabetes and/or hypertension associated with increasing BMI in Saudi adults, Eastern province, 2004, based on regression analysis (n=195851).

BMI	Diabetes odds ratio (95% CI)		Hypertension odds ratio (95% CI)		Diabetes and hypertension odds ratio (95% CI)		Diabetes or hypertension odds ratio (95% CI)	
	Men	Women	Men	Women	Men	Women	Men	Women
21	1.43* (1.16-1.78)	1.28 (0.98-1.67)	1.15 (0.89-1.48)	1.05 (0.82-1.34)	1.47 (0.93-2.30)	1.64 (1.09-2.45)	1.30* (1.08-1.55)	1.05 (0.86-1.29)
22	1.67* (1.38-2.03)	1.63* (1.29-2.05)	1.11 (0.88-1.41)	1.22 (0.98-1.50)	1.59 (1.06-2.40)	1.59 (1.10-2.32)	1.41* (1.20-1.66)	1.37* (1.15-1.63)
23	1.99* (1.67-2.38)	2.00* 1.63-2.47)	1.53* (1.25-1.87)	1.34* (1.10-1.62)	2.21* (1.53-3.17)	2.23* (1.59-3.11)	1.76* (1.53-2.04)	1.53* (1.30-1.79)
24	2.22* (1.88-2.63)	1.99* (1.63-2.44)	1.69* (1.40-2.05)	1.55* (1.29-1.86)	2.47* (1.74-3.49)	2.14* (1.55-2.97)	1.98* (1.72-2.27)	1.70* (1.46-1.97)
25	2.43* (2.07-2.86)	2.71* (2.24-3.28)	2.00* (1.66-2.38)	1.80* (1.51-2.13)	3.02* (2.16-4.21)	2.86* (2.10-3.89)	2.20* (1.93-2.51)	2.12* (1.84-2.45)
26	2.80* (2.39-3.28)	2.85* (2.34-3.44)	2.08* (1.74-2.49)	1.84* (1.55-2.19)	3.26* (2.35-4.53)	2.79* (2.06-3.79)	2.47* (2.17-2.81)	2.25* (1.95-2.59)
27	2.76* (2.36-3.23)	2.85* (2.36-3.44)	2.45* (2.06-2.92)	2.03* (1.72-2.40)	3.69* (2.67-5.12)	3.56* (2.64-4.79)	2.59* (2.28-2.95)	2.51* (2.19-2.88)
28	3.01* (2.57-3.51)	3.37* (2.80-4.05)	2.72* (2.29-3.24)	2.27* (1.93-2.67)	4.54* (3.29-6.26)	4.27* (3.19-5.71)	2.78* (2.45-3.16)	2.85* (2.49-3.27)
29	3.25* (2.78-3.80)	3.94* (3.29-4.73)	2.90* (2.43-3.45)	2.54* (2.16-2.99)	4.31* (3.11-5.95)	4.32* (3.23-5.79)	3.11* (2.74-3.54)	3.39* (2.96-3.88)
30	3.35* (2.87-3.92)	4.50* (3.76-5.39)	3.07* (2.58-3.65)	2.80* (2.39-3.29)	4.77* (3.46-6.59)	4.66* (3.48-6.22)	3.20* (2.82-3.64)	3.68* (3.22-4.20)
31	3.46* (2.96-4.05)	4.73* (3.96-5.66)	3.60* (3.02-4.28)	3.00* (2.56-3.52)	5.89* (4.28-8.12)	5.23* (3.92-6.99)	3.40* (3.00-3.87)	3.79* (3.324.34)

*Odds of disease significant (*P*<.001) when compared with BMI < 20 as a reference group

ROC curve analysis showed that the corresponding sensitivities and specificities were poor (<0.63 and <0.62, respectively). This indicates that the percentage of people identified as having the risk factors and the percentage of people who were identified as not being at risk were less than 63% of total population. Both LR+ and LR− were close to 1.0, indicating a minimal increase in the likelihood of the presence of the risk factor if the test is positive and a minimal decrease in the
ihood if the test is negative. PPVs were small and
om 0.08-0.25. This indicates that the propor-
eight and obese people who were classified
eight or obese was <25%. On other
f non-overweight or non-obese
correctly were ranged from
NPVs. The FP and FN
other in both women
ssification was very high and exceeded 80% of the total population across all the selected BMI cut-off points.

The technical statistical term "diagnostic performance" has been used to characterize the relationship between BMI and presence of diabetes or hypertension. This does not mean that BMI is used a diagnostic clinical test for these conditions. However, clinicians will generally be more concerned about false negatives, when patients at risk may be overlooked for treatment. By using BMI as a tool for assessing the metabolic risks of being overweight or obese, these findings suggest that 37% to 45% of people with risk factors would be incorrectly identified as healthy, as indicated by the FN rate. The percentage varies depending on the risk factors being studied. This finding is also supported by the high values of specificities and NPVs and the values of LR-. The use of the higher BMI cut-off values suggested by the ROC analysis (Table 2) would misclassify large

Table 4. Diagnostic performance of BMI in detecting diabetes and/or hypertension using optimal BMI cut-off values based on the significant association using logistic regression in Saudi adults, Eastern province, 2004, (n=195851).

Risk factors	Gender	n	AUC (95% CI)	Cut-offs kg/m²	Sensitivity	Specificity	PPV	NPV	LR +	LR -	FP rate	FN rate	Misclassification rate
Diabetes	Men	99946	0.566 (0.561-0.571)	21	0.98	0.06	0.16	0.94	1.04	0.33	0.94	0.02	0.96
	Women	95905	0.618 (0.614-0.622)	22	0.98	0.08	0.20	0.95	1.07	0.25	0.92	0.02	0.94
Hypertension	Men	99946	0.625 (0.62-0.63)	23	0.95	0.13	0.14	0.95	1.09	0.38	0.87	0.05	0.92
	Women	95905	0.645 (0.641-0.650)	23	0.96	0.12	0.19	0.93	1.09	0.33	0.88	0.04	0.92
Diabetes or Hypertension	Men	99946	0.594 (0.590-0.598)	21	0.98	0.06	0.11	0.96	1.04	0.33	0.94	0.02	0.96
	Women	95905	0.640 (0.636-0.643)	22	0.97	0.09	0.13	0.95	1.07	0.33	0.91	0.03	0.94
Diabetes and Hypertension	Men	99946	0.618 (0.611-0.625)	23	0.96	0.12	0.06	0.98	1.09	0.33	0.88	0.04	0.92
	Women	95905	0.643 (0.637-0.649)	23	0.97	0.11	0.09	0.98	1.09	0.33	0.89	0.03	0.92

AUC: area under the curve; PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio; LR-: negative likelihood ratio; FP rate: false positive rate; FN rate: false negative rate.

percentages of people with risk factors as being healthy who might then miss the opportunity for treatment.

To reduce the large chance of such misclassification, we attempted to identify cut-offs based on the observed significant association between BMI and risk factors. Regression analysis showed that the risk of diabetes and/or hypertension was significantly increased at BMI values as low as 21-23 and increased progressively as BMI increased. Applying this criterion to identify the cut-off values resulted in improvements in sensitivity, NPV, LR-, FN and worsening in specificity, PPV, LR+, FP and the overall misclassification rate. Using these lower BMI cut-offs resulted in a very small FN rate ranging from 0.02 to 0.05. Therefore, most people with risk factors were correctly identified as at risk. This finding may suggest obesity management should be considered even at a quite low BMI values in the Saudi population.

This is not the first study to suggest the presence of a significantly increased risk of co-morbidities at BMI values less than 25. In a Chinese population in Hong Kong, diabetes and hypertension were also reported to increase from a BMI value of 22 onwards.[38] However, the use of such low cut-offs would lead to large misclassification of healthy people as being at risk, as indicted by the high values of sensitivities and FP rates. This fact that could cause unnecessary and costly diagnostic testing. Overall the total misclassification rate was unacceptably high, even with the use of different BMI cut off points and different selection criteria, and even with the use of the recommended value by WHO (BMI=25). These findings illustrate the significant limitations in using BMI alone for obesity diagnosis in the Saudi Arabian population.

To our knowledge, only one study has assessed the optimal BMI cut-off points on a sample of the Arab population of the Middle East, which was conducted in 1420 Omani adult subjects.[32,33] The authors analyzed that study using two different definitions of cardiovascular disease (CVD) risk. When CVD risk was identified as the presence of at least two out of three risk factors (hyperglycemia, hypertension and dyslipidemia), the optimal BMI cut-off points for men and women were 23.2 and 26.8, respectively.[32] Using the Framingham risk score, the optimal cut-off points for men and women were 22.6 and 22.9, respectively.[33] The use of the first definition resulted in moderate sensitivity (71.0) and poor specificity (53.7) with AUC of 0.65 in men and poor sensitivity (46.8) and moderate specificity (76.5) with AUC of 0.66 in women. Using the Framingham risk score resulted in good sensitivity (80.3), very poor specificity (37.3) and AUC of 0.60 in men, and good sensitivity (84.2), poor specificity (45.1) and AUC of 0.64 in women. Both methods indicated that waist-to-hip ratio (WHR) and waist circumference (WC) were better surrogates to detect CVD risk compared to BMI. One major limitation of that study was the small sample size, which may limit the generalizability of the findings to other Middle Eastern populations. Unfortunately, other diagnostic characteristics of BMI as a tool for obesity diagnosis were not calculated.

Most of the other previous studies that have been conducted in non-Caucasian populations did not assess the misclassification rate.[15,24,32-38] However, one study conducted in Asian Indians also indicated a high overall misclassification rate, particularly in women.[39] Those authors concluded that the BMI did not accurately predict overweight in that population.

Several reasons may explain the weakness of BMI as a tool to classify obesity in the Saudi Arabian population. First, BMI does not reflect fatness uniformly in all populations and different ethnic groups.[9,39-41] The previous Omani study indicated that WHR and WC better predict CVD risk than BMI.[32,33] This may suggest the importance of including a measure of abdominal obesity in classifying obesity in Middle East populations such as those in Oman and Saudi Arabia. Second, the short stature of Saudi women could be limiting the usefulness of BMI in this population.

Strengths and limitations of this study should be recognized. The very large number of participants provided sufficient cases at each single unit of BMI to assess the significance of association between each BMI unit and the presence of diabetes or hypertension. In contrast, the cross-sectional nature of the survey and the absence of measurements of other relevant obesity-related co-morbidities, such as hypercholesterolemia and hypertriglyceridemia, could be considered as limitations in this study. The sample was a convenience non-random sample. However, it is fairly representative of the target population. When we compared the sub-classification of respondents with the latest census done in the eastern province regarding to age and sex, the characteristics of the study sample were similar.[20] The relatively low response rate of participants coming for the confirmatory diagnostic test and the reliance on a single screening test using capillary blood glucose may have had an effect on the low performance of BMI in predicting diabetes and hypertension in this study. Also the relatively high values chosen for the definition of diabetes and hypertension for participants who did not come for the confirmatory test may have had a similar negative effect on the performance of BMI. However, >70% of participants who did not come for the confirmatory test for diabetes had IFG or IGT based on CFBS and CRBS. The situation was also similar for hypertension. Whether similar conclusions would be reached had this study been done on a random sample with avoidance of the above-mentioned limitations or not remains to be seen in future studies. Similarly, it is not clear if such conclusion would be obtained in a national sample covering other regions of Saudi Arabia.

In conclusion, the diagnostic usefulness of BMI alone in defining obesity is limited in this large population of Saudi adults in the Eastern Province, for both men and women. Future studies incorporating other measures such as WC, WHR, body fat composition, or a combination of tools, need to be conducted to determine the best method to classify obesity accurately in the Saudi population. It seems likely however that limiting management of obesity to those individuals with a BMI>30 may mean that many Saudis at risk of serious co-morbidities could be missing necessary interventions.

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Inferior vena caval filters: 5 years of experience in a tertiary care center

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Ann Saudi Med 2009; 29(6): 446-449

PMID: 19847081 DOI: 10.4103/0256-4947.57166

BACKGROUND AND OBJECTIVES: Interruption of the Inferior Vena Cava (IVC) is recommended in certain cases to prevent Pulmonary Embolism (PE). Reported data on the efficacy and rate of complications vary considerably.

PATIENTS AND METHODS: We conducted a retrospective analysis of patients who had a temporary or permanent IVC filter inserted at our institution during the past 5 years.

RESULTS: Seventy-seven of 225 patients (34%) with Venous Thrombosis (VT) had an IVC filter inserted. Deep vein thrombosis and PE were the most common causes for anticoagulation. Bleeding was the reason for IVC filter insertion in 48 (62%). The only complication found was the breaking of a temporary filter during removal related to the procedure. However, 3 patients (out of 10) had a recurrence of VT after prolonged discontinuation of anticoagulation.

CONCLUSIONS: Our criteria for indication of IVC filter insertion are in line with current standard of care. The immediate and delayed complications caused by IVC filter insertion was low. Active bleeding was the most common indication for filter insertion, whereas inherited thrombophilia was relatively common.

Venous thromboembolism (VTE) is a significant cause of morbidity and mortality. Pulmonary embolism (PE) is the most serious complication of VTE. It affects more than 350 000 patients in the USA annually and results in as many as 240 000 deaths per year.[1] Despite improvement in diagnosis and management, the average annual incidence of VTE in communities has remained stable.[2] Pulmonary embolism is usually managed with anticoagulation therapy.[3] Thrombolysis is used for massive and sometimes for submassive PE. When pharmacological therapy fails, or is contraindicated, or in situations where a small additional PE can cause significant deterioration or even death, then interruption of the inferior vena cava (IVC) is recommended.[4]

Mechanical interruption of blood flow as a mean of preventing PE has a long history. Femoral vein ligation first performed by John Junter in 1874, and later advocated by Homans in 1934, failed to prevent PE.[5] IVC ligation was later tried, but caused major complications.[6] Mobin-Ubbin filter, the first intraluminal umberella led to significant thrombosis and migration.[7] In 1973, the Greenfield filter was inserted percutaneously.[7] Its success was followed by the introduction of several other IVC filters, but the "ideal device" is yet to be found. The recommendations by the Seventh American College of Chest Physicians Conference on Antithrombotic Therapy for IVC filter use states that 1) for most patients with deep vein thrombosis (DVT), routine use of IVC filter is not indicated and 2) placement of an IVC filter is suggested in patients with a contraindication to or a complication of anticoagulation, as well as in those with recurrent thromboembolism despite adequate anticoagulation.[4] Other less common indications include chronic recurrent PE with severe pulmonary hypertension in patients undergoing surgical embelectomy/endarterectomy, and in patients with a free-floating ileocaval clot.

Data on the efficacy and complications for each filter suffer many limitations and show extreme variability in different series.[9] It is therefore important that each center look at their own experience with IVC filter insertion and incorporate that into the decision-making process for using such devices. Our objective was to study our experience with IVC filters by looking at the types of filters inserted, the reasons for insertion, complication rates and the safety and efficacy of IVC filters.

PATIENTS AND METHODS

We conducted a retrospective analysis of patients who had a temporary or permanent filter inserted at King Faisal Specialist Hospital and Research Centre in the past 5 years (2002-2007). The study was approved by the Institute Research Advisory Council and the Bioethics Committee. A "Data Acquisition Form" was developed by the investigators that allowed the incorporation of all relevant data. The complications recorded included radiological complications, bleeding, hematoma, failure of insertion, infection, migration and thromboembolism.

RESULTS

Seventy-seven patients were identified, including 42 males (54.5%) and 35 females (45.5%). Sixty-six patients (85.7%) were Saudis and 11 (14.3%) were of mixed nationalities. Forty-five patients (58.4%) were followed for 5 years, seven patients (9%) for four years. Ten were lost to follow-up, five of whom had cancer and who lived outside Riyadh and probably died. The minimal follow-up period for these 10 patients was six months during which no complications related to the IVC filter were reported. Sixteen patients died, with sepsis, multiorgan failure or cancer within two weeks of the IVC filter insertion. The majority (14/16) died while in the intensive care unit.

Of the 77 IVC filters inserted, 50 were permanent filters and 27 were temporary. Twenty of the 27 temporary filters (74.1%) were inserted in patients with active bleeding (20/77). Seven temporary filters (25.9%) were inserted to protect a high-risk patient from future PE, usually as a perioperative measure. Of the 27 temporary IVC filters inserted, fourteen (51.9%) were later removed.

The reason(s) for anticoagulation is shown in Table 1- some patients had more than one reason for anticoagulation. Table 2 shows the reason for inserting an IVC filter, the most common being major bleeds. Table 3 shows the site of these major bleeds. Table 4 shows the risk factor(s) for venous thrombosis. Most patients had more than one risk factor. The most common risk factor was immobility (41.55%). The reason for immobility was mostly the post-operative period after major surgery (62%), followed by multiple injuries secondary to trauma (37%).

Seventeen patients out of the 60 (28%) studied (28%) had a hypercoagulable state as shown in Table 5.

Anticoagulation therapy was continued after the IVC filter insertion in 22/77 patients (28.5%). All except two had warfarin given to a target INR 2.0-3.0. Two were initially given low molecular weight heparin and later changed to warfarin. Fifty-five (71.5%) patients had their anticoagulation therapy discontinued or not started at all after the IVC insertion because of

Table 1. Reasons for anticoagulation in 77 patients who had IVC filters.

Reason for anticoagulation*	Number of cases
Deep vein thrombosis	27 (35%)
Pulmonary embolism	22 (28%)
Recurrent deep vein thrombosis	5 (6.0%)
Recurrent pulmonary embolism	3 (4%)
Recurrent deep vein thrombosis and pulmonary embolism	8 (10.4%)
Portal vein thrombosis	1 (1.3%)
Inferior vena caval thrombosis	1 (1.3%)
Severe pulmonary hypertension	1 (1.3%)
Deep vein thrombosis prophylaxis	5 (6.0%)
Others	7 (9%)

*Some patients had more than one reason for anticoagulation

Table 2. Reasons for IVC filter insertion.

Reason for insertion of IVC filter	Number of cases (%)
Bleeding	48 (62%)
Pre-operative insertion in patients with high risk of venous thrombosis	12 (15.6%)
Pre-thrombectomy	2 (2.6%)
Severe pulmonary hypertension	2 (2.6%)
Severe thrombocytopenia	1 (1.3%)
Recurrent deep vein thrombosis (despite anticoagulation)	4 (5.1%)
Post-operative deep vein thrombosis (high risk of bleeding)	4 (5.1%)
Post-operative pulmonary embolism (high risk of bleeding)	3 (3.9%)
Heparin-induced thrombocytopenia	1 (1.3%)
Total	**77**

Table 3. Sites of bleeding in patients with IVC filters.

Site of bleeding	Number of cases (%)
Gastrointestinal tract	17 (35.4%)
Intracerebral	9 (18.7%)
Subdural	2 (4.1%)
Subarachoid	1 (2%)
Hematuria	4 (8.3%)
Intraabdominal	1 (2%)
Reteroperitoneal	4 (8.3%)
Pulmonary	1 (2%)
Lower limb	1 (2%)
Tracheostomy	1 (2%)
Vaginal	2 (4.1%)
Multiple Sites	5 (10.4%)
Total	**48**

Table 4. Risk factors for venous thrombosis in patients with IVC filters.

Risk factor*	Number of cases (%)
Immobility	32
Cancer	26
Post-operative period	20
Trauma	12
Hypercoagulate state	12
Heart failure	5
Critical illness	4
Morbid obesity	4
Stroke	3
Drug abuse	2
Pregnancy	1
HIT	1

*Some patients had more than one risk factor

active bleeding in 48/55 (87%) or a perceived high risk of bleeding if anticoagulants were to be used in 7/55 (12.7%). Of these patients whose anticoagulation therapy was initially discontinued, 45/55 (82%) had their anticoagulation therapy resumed within 10 days as the reason resolved for withholding anticoagulation. Ten patients remained off anticoagulant therapy; 3 developed VT (30%). One was diagnosed with a clot on the IVC, and 2 developed lower limb DVT. In one instance the temporary filter broke during removal and had to be surgically removed. There were no instances of migration, infection or perforation, or death directly related to the procedure.

DISCUSSION

A recent extensive review of IVC filters showed a widespread variation in complications.[10] While death due to IVC filter (0.12%) and fatal PE (0.7%) was small, PE post-filter insertion varied from 2% to 5%. Filter fracture (1%) and guide wire entrapment (<1%) were also universally rare. On the other hand, complications from insertion including bleeding, infection, pnuemothorax, stroke, air embolism, filter malposition and malfunction varied considerably, from 4% to 11%. Furthermore the rate of migration of the filter (3% to 69%), penetration of the IVC (9% to 24%), venous access site thrombosis (2% to 28%), obstruction of the IVC (6% to 30%) and venous insufficiency (5% to 59%) showed marked variation.[10,11] Reporting thrombosis of IVC filters has been particularly nonuniform and depends on whether or not all patients (as opposed to only symptomatic patients) were studied, the method of investigating possible thrombosis and the duration of follow up.Reports vary widely from 0% to 28%.[11]

This review shows that the practice of IVC filter insertion at our institution, as far as the indications are concerned, are consistent with the accepted recommendations and standard of care.[4] The vast majority of patients had a contraindication, complication or failure of anticoagulation therapy (52/77). There was however, some unique features in our study population. The preventive IVC filter insertion pre-operatively in the high-risk patients (including two pre-embelectomy procedures) is testament to the high-risk population encountered in a tertiary (compared to a primary of secondary) care hospital. Furthernore, patients with an IVC Filter insertion had a more serious thromboembolic disease with 50% having PE. They also had more serious comorbid conditions with 16/77 (21%) dying of sepsis and multiorgan failure or advanced cancer and none of thomboembolic complications. The vast majority who

Table 5. Results of thrombophilia testing (n=60).

Test for thrombophilia	Number of cases*
Primary antiphospholid syndrome	5 (8.3%)
Secondary antiphospholipid syndrome	2 (3.3%)
Anti β_2 glycoprotein	1 (1.7%)
Factor V Leiden (heterozygous)	3 (5%)
Prothrombin 20210G>A mutant gene (heterozygous)	1 (1.7%)
Protein S deficiency	3 (5%)
Antithrombin III deficiency	2 (3.3%)
Protein C deficiency	1 (1.7%)
Essential thrombocytosis	1 (1.7%)
Total	**19 (32%)**

*Some patient had more than one risk factor

died (14/16) were in intensive care unit. Bleeding was the most common cause of IVC filter insertion (63%) as in other series. However, there was a relatively large number of patients with central nervous system bleeds (26% of the total bleeds) which relates to an active neurosurgical program at this center.

Our rate of immediate and delayed complications caused by the IVC filter insertion was reassuringly low and should allow us to be more liberal in using the filters, but only for well-defined and accepted indications. One instance of a break in the tip of the filter was the only complication of the procedure per se. However there was a 30% chance of recurrence of VT when an IVC filter was inserted and anticoagulation therapy was discontinued indefinitely and this confirms the need for long-term anticoagulation post-IVC filter insertion.[12]

The number of patients who tested positive for thrombophilia was astonishingly high and requires further study. It is possible that the protein C and protein S deficiency may be acquired (because of Warfarin therapy or other diseases, rather than genetic). However, even if all protein C and S deficient patients are considered to be acquired, we still have a 20% prevalence. Our data from more than 800 healthy Saudi individuals showed a very low incidence of familial thrombophilia.[13] To our knowledge this is the first report on IVC filters in Saudi Arabia and the Gulf. Our data represent 186 patient-years of experience.

Acknowledgment

The authors would like to extend their deep appreciation for Dr. Muneerah Al-Bugami for reviewing the manuscript.

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original article

Renal biopsy in patients with type 2 diabetes mellitus: indications and nature of the lesions

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Ann Saudi Med 2009; 29(6): 450-453

PMID: 19847082 DOI: 10.4103/0256-4947.57167

BACKGROUND AND OBJECTIVES: The prevalence of non diabetic renal disease (NDRD) among patients with type 2 diabetes mellitus varies widely depending on the selection criteria and the populations being studied. The aim of this study was to evaluate the renal biopsies performed on type 2 diabetic patients for suspicion of NDRD and to correlate the pathological with the clinical and laboratory findings.

SUBJECTS AND METHODS: We selected and reviewed biopsies performed on type 2 diabetics for clinically suspected NDRD from January 2006 to December 2008 at a single hospital. Clinical and laboratory data were analyzed in relation to the histopathology findings. Patients were grouped into either group I with isolated DGS or group II with NDRD on top of DGS.

RESULTS: Thirty-one biopsies were performed on type 2 diabetic patients; Seventeen patients (54.8%) were males. Mean age was 50.68 (11.29) years. The mean duration of diabetes was 9.33 (3.6) years. Renal biopsy showed that among the studied group 14 patients (45.2%) showed NDRD on top of DGS. Crescentic glomerulonephritis was the commonest finding seen in 3 cases (21.4% of group II cases) followed by acute tubulointerstitial nephritis and hypertensive changes each was seen in 2 cases (14.4%). Other findings included IgA nephropathy, primary focal segmental glomerulosclerosis, rhabdomyolysis, membranoproliferative glomerulonephritis each of them was seen in one case (7.1%). Group I had a significantly higher level of proteinuria 4.97 (2.08) gm/24 hrs urine than group II 2.72 (1.09) gm/24 hrs urine (P=.003). There was no significant difference between the two groups in age, duration of diabetes, gender, presence of hypertension, hematuria, serum creatinine or glomerular filtration rate.

CONCLUSION: The present study showed that crescentic glomerulonephritis is the commonest NDRD among diabetic patients. A higher level of proteinuria was reported among those with NDRD superimposed on DGS. So, Renal biopsy should be performed in diabetics when the clinical scenario is atypical.

Diabetic nephropathy (DN) is characterized by persistent proteinuria, hypertension, and a progressive decline in renal function.[1] About 20% to 40% of patients suffering from diabetes mellitus eventually develop diabetic renal disease.[2] It accounts for over 40% of new cases of end-stage renal disease (ESRD) annually, and is considered the leading cause of ESRD in the USA as well as Europe and Japan.[2] The characteristic lesion of DN is nodular glomerulosclerosis, as described by Kimmelstiel and Wilson.[3] Renal diseases other than DN can occur in diabetic patients. The absence of retinopathy or neuropathy in patients with evidence of nephropathy may imply that the underlying pathology is unrelated to diabetes.[4] Other clinical predictors of non-diabetic renal disease (NDRD) in diabetic patients include rapid deterioration of renal function, and microscopic or macroscopic hematuria.[5] A renal biopsy is not routinely performed in diabetic patients. It is indicated however, in patients where NDRD is suspected.[5-7] The aim of this study was to evaluate the renal biopsies performed on patients with type 2 diabetes for suspicion of NDRD and to correlate the pathology findings with the clinical presentation and laboratory parameters.

SUBJECTS AND METHODS

All native kidney biopsies performed at Mubarak Al

Kabeer Hospital from January 2006 to December 2008 were retrospectively reviewed. Biopsies performed on patients with type 2 diabetes for clinically suspected NDRD were selected and reviewed. Biopsy indications were the presence of Microscopic hematuria, proteinuria without retinopathy or unexplained rapid worsening of renal function. All patients underwent ultrasound-guided renal biopsy using a gauge 16 coaxial quick-core biopsy set. Written consent was obtained from each patient prior to the procedure. The histopathology glass slides were reviewed and the pathology reports were retrieved from the department of pathology computerized filing system. Each kidney biopsy was prepared by cutting paraffin blocks at 3 um sections and staining 2 slides with peroidic acid schiff, 2 slides for hematoxylin and eosin, 1 slide for Jones Methenamine sliver and one slide for trichrome. Immunoperoxidase staining was also performed routinely on all slides for IgG, IgA, IgM and C3. Antibodies were from Dako and titration was performed according to the leaflets with the antibody vials. Electron Microscopy (EM) is not routinely done on all cases in our institution, however, on selected cases EM was performed and the films were retrieved and reviewed along with the EM report.

Patients were grouped by isolated diabetic glomerulosclerosis (DGS) (group I) and by NDRD on a background of DGS (group II). Non of the studied population had isolated NDRD. Patient data including age, gender, duration of diabetes, presence of retinopathy on fundus examination, presence of hypertension (defined as systolic blood pressure above 140 mm Hg, or diastolic blood pressure above 80 mm Hg or intake of antihypertensive medications) were included. Serum creatinine, glomerular filtration rate as estimated by MDRD (modifecation of diet in renal disease study) formula,[8] presence of hematuria defined as 2 or more red blood cells per high-power field in a centrifuged urine sample prior to biopsy,[9] and proteinuria using 24 hours urine protein were all considered.

The differences between the two groups were assessed using the χ^2 test for categorical variables and the nonparametric Mann Whitney U test for continuous variables. Significance was evaluated using a two sided $P<.05$. Statistical analysis was performed using SPSS for windows version 16 (SPSS, Inc, Chicago, IL)

RESULTS

A total of 312 renal biopsies from native kidneys done during the study period, 31 (9.9%) were performed on patients with type 2 diabetes. Seventeen (54.8%) patients were males. Their mean age was 50.68 (11.29) years. The mean duration of diabetes was 9.33 (3.6) years (Table 1). Indications for renal biopsy were the presence of hematuria in 15 (48.4%) patients, unexplained rapid deterioration of renal function in 10 (32.26%) patients and sudden onset of massive proteinuria without retinopathy in 6 (19.3%) cases. Renal biopsy should that among the studied population 17 (54.8%) cases were found to have isolated diabetic glomerulosclerosis whereas the remaining 14 (45.2%) subjects had nondiabetic renal diseases superimposed on diabetic glomerulosclerosis (Figures 1 and 2).

Histopathological findings in group II patients showed pauci-immune crescentic glomerulonephritis as the commonest finding seen in three cases (21.4%), acute tubulointerstitial nephritis and hypertensive changes each in 2 cases (14.3%), IgA nephropathy with mesangial IgA deposits in one case (7.1%), immune complex mediated membranoproliferative glomerulonephritis (MPGN) with immune deposits of C3, IgM and IgG in the mesangium and peripheral capillary

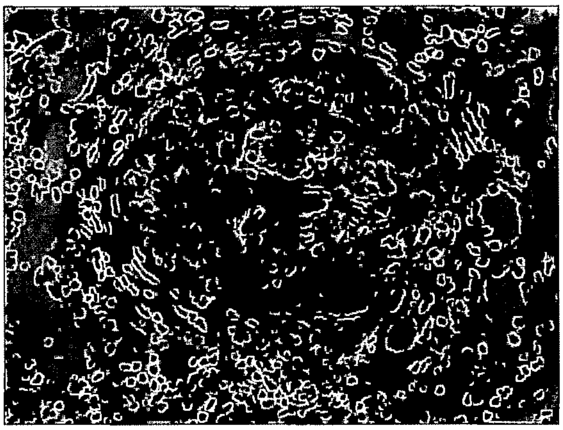

Figure 1. A cellular crescent is present with disruption of the Bowman's space (hematoxylin-eosin stain ×200).

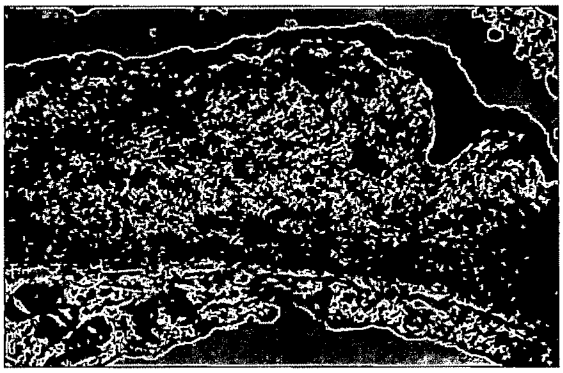

Figure 2. Fibrillary EM; randomly arranged fibrils deposited within the glomerular basement membrane (EM ×80 000).

Table 1. Clinical and laboratory data for the studied diabetic patients (n=31).

Patient characteristics	
Age in years mean (SD)	50.68 (11.29)
Male gender (%)	17 (54.8)
Hypertension (%)	17 (54.8)
Retinopathy (%)	14 (45.2)
Duration of diabetes in years mean (SD)	9.33 (3.6)
Creatinine μmol/L mean (SD)	395.23 (299.8)
GFR ml/min/1.73 m² mean (SD)	38.6 (21.0)
Urinary proteins gm/24 hours mean (SD)	3.18 (1.6)
Hematuria (%)	15 (48.4)

Table 2. Histopathological findings in group II (n=14).

Histopathological findings	Number of patients (%)
Crescentic glomerulonephritis	3 (21.4)
Acute tubulointerstitial nephritis	2 (14.3)
Hypertensive changes	2 (14.3)
IgA nephropathy	1 (7.1)
Granulomatous interstitial nephritis	1 (7.1)
Fibrillary glomerulonephritis	1 (7.1)
Primary focal segmental glomerulosclerosis	1 (7.1)
Immune complex mediated membranoproliferative glomerulonephritis	1 (7.1)
Tubular injury secondary to rhabdomyolysis	1 (7.1)
Acute pyelonephritis	1 (7.1)

loops in one case (7.1%), fibrillary glomerulonephritis with mesangial deposits of C3, IgG, IgA and IgM was seen in one patient (7.1%). Other pathological findings are summarized in Table 2. Group I was found to have a significantly higher level of proteinuria than group II (*P*=.003). Retinopathy was significantly higher in group I than in group II (*P*=.008, OR=8.8, CI [1.69-45.76]). No statistically significant difference was detected between the two groups in age at time of biopsy (*P*=.49), duration of diabetes (*P*=.17), gender (*P*=.1), presence of hypertension (*P*=.12), hematuria (*P*=.1), creatinine level (*P*=.86) or creatinine clearance at time of presentation (*P*=.74) (Table 3).

DISCUSSION

Diabetic nephropathy is one of the most frequent and clinically important complications of diabetes, affecting approximately 40% of patients who have had diabetes for more than 20 years and contributing to a substantial number of patients entering into ESRD programs.[10] Among patients with type 2 diabetes the prevalence of NDRD varies widely depending on the selection criteria and the populations being studied.[6,11] The frequency of NDRD in diabetics has been reported to be 7 to 44%.[11]

In the present study NDRD was detected in 45.8% of biopsies of diabetic patients. This was in accordance with previous studies where the prevalence of NDRD was found to range from 45% to 57%,[6,12-14] but different from other studies where the prevalence of NDRD was around 7-10%.[15,16] This low prevalence could be explained by the different selection criteria for doing renal biopsy in such patients. In the present study no significant difference was found between the two groups in age at the time of biopsy. In contrast, Soni et al[10] reported that patients with NDRD on the background of DGS were older than those with isolated DGS. The present study did not show a significant difference in the duration of diabetes between the two groups. This was in accordance with Bertani et al[11] whereas, Soni et al[10] reported a shorter duration of diabetes with NDRD. Our study was in accordance with the previous study that showed no significant difference in the incidence of associated hypertension between the two groups.[10] There was also no significant difference between the two studied groups in serum creatinine or creatinine clearance. This was in contrast to the results of Soni et al[10] and Taft et al[17] where azotemia was higher in patients with NDRD on top of DGS. Our results were in accordance with previous studies that showed a significantly higher proteinuria in patients with DGS than in patients with NDRD on top of DGS.[6,10] Also, the present study agrees with Pham et al[7] in showing that hematuria is not a useful predictor of diabetic or non-diabetic renal disease. Our study confirmed the accepted view that one of the important predictors of NDRD is the absence of retinopathy.[10,13,18] However, the presence of retinopathy should not rule out the need for renal biopsy, especially if the clinical scenario is atypical. Our study showed that crescentic glomerulonephritis was the commonest NDRD detected in the studied biopsies, whereas Soni et al[10] reported that acute tubulointerstitial nephritis and postinfectiuos glomerulonephritis were the commonest NDRD. IgA nephropathy was found to be the commonest NDRD in other studies.[19,20]

The mechanism implicated in the development of

NDRD in diabetic patients remains speculative. The predisposition of DGS to superimposed nephritis has been attributed to enhanced exposure of antigenic cellular components that triggers immune responses. Also, pre-existing glomerular alterations might favor an immune reaction in the subepithelial space.[10] Lai et al[21] however, found no difference in the prevalence of NDRD between patients with and without diabetes and that the coexistence of a different glomerulonephritis in the diabetic kidney might be coincidental.

In conclusion, the present study showed that non NDRD was seen in 45.2% of the studied diabetic population and crescentic glomerulonephritis is the commonest NDRD among diabetic patients. A higher level of proteinuria was reported among those with NDRD superimposed on DGS. So, conducting a renal biopsy in diabetic patients is important when the clinical scenario is not typical of diabetic nephropathy as many of the pathological lesions found in our group of patients had the potential for treatment with agents other than the standard angiotensin converting enzyme inhibitors or angiotensin receptor blockers commonly used in typical DGS. Our study has some limitations. It was a retrospective single centre study that included a small number of patients from the same geographical area. A more longitudinal study needs to be done on a larger number of diabetic patients to evaluate the actual prevalence of NDRD in diabetic patients.

Table 3. Comparison of patients with isolated diabetic glomerulosclerosis (group 1) and patients with non diabetic lesions on top of diabetic glomerulosclerosis (group II) in the demographic, clinical and laboratory characteristics.

Parameter	Group I (DGS)	Group II NDRD	*P* value
Age in years mean (SD)	52.13 (13.2)	49.3 (9.4)	>.05
Male gender (%)	9 (64.3)	8 (47.05)	>.05
Hypertension (%)	8 (50)	9 (60)	>.05
Retinopathy (%)	11 (68.8)	3 (20)	.008
Duration of diabetes in years mean (SD)	10.06 (3.31)	8.27 (3.8)	>.05
Serum creatinine µmol/L mean (SD)	395.56 (335.09)	376.2 (266.58)	>.05
GFR ml/min/1.73 m^2 mean (SD)	35.21 (17.5)	41.7 (15.02)	>.05
Urinary proteins g/24 hours mean (SD)	4.97 (2.08)	2.72 (1.09)	.003
Hematuria (%)	7 (43.8)	8 (53.3)	>.05

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original article

Clinical characteristics and computed tomography findings in Arab patients diagnosed with pulmonary sarcoidosis

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Ann Saudi Med 2009; 29(6): 454-459
PMID: 19847083 DOI: 10.4103/0256-4947.57168

BACKGROUND AND OBJECTIVE: Sarcoidosis is prevalent worldwide with significant heterogeneity across different ethnic groups. We aimed To describe the clinical characteristics and computed tomography findings among Arab patients with pulmonary sarcoidosis.

METHODS: A retrospective study of patient demographics, symptoms, co-morbid illness, sarcoidosis stage, treatment, pulmonary function and CT results.

RESULTS: Of 104 patients, most (77%) were 40 years of age or older at diagnosis, and females in this category (≥40 years) significantly outnumbered male patients (69/104 (66.3%) vs. 35/104 (33.7%), *P*=.003). The most common complaints were dyspnea (76%), cough (72.1%) and weight loss (32.7%). The majority of patients displayed impairment in lung function parameters at presentation. However, significant impairment in forced vital capacity, percentage predicted (FVC%) (<50%) was present in only 17% of patients. The most frequent CT finding was mediastinal lymph node enlargement in 49 patients (73.1%). Parenchymal abnormalities indicating lung fibrosis were noted in 31 patients (46.3%), and traction bronchiectasis was the most common (35.8%) fibrotic pattern detected on CT scans.

CONCLUSION: At presentation, clinical manifestations of sarcoidosis among this sample of Arab patients were similar to reports from other nations. Further studies are needed to explore the effects of race and ethnicity on disease severity in the Middle East.

Sarcoidosis is a granulomatous disease of unknown etiology that most commonly affects the lungs and intrathoracic lymph nodes, but also has protean extrapulmonary manifestations. The disease is prevalent worldwide. However, significant heterogeneity in the frequency, clinical characteristics and severity of disease is observed across different ethnic groups and between the genders.[1-5] Furthermore, radiographic findings at the time of diagnosis and the rate of radiographic clearing with treatment were also different among different ethnic groups.[5] Limited reports on sarcoidosis in Arab patients have appeared,[6-8] and to the best of our knowledge, no specific study has described CT findings among Arab patients diagnosed with pulmonary sarcoidosis. This retrospective study was conducted to explore the clinical, physiological, and radiological characteristics of pulmonary sarcoidosis in a sample of Arab patients.

METHODS

We conducted a retrospective review of all patients diagnosed with biopsy-proven pulmonary sarcoidosis at three centers (King Khalid University Hospital, King Abdulaziz Medical City and Riyadh Military Hospital) in Riyadh, Saudi Arabia, between January 1992 and December 2007. Patients were identified from the records of outpatient pulmonary clinics and hospital medical departments. This investigation was approved by the ethics committee of each participating hospital. Sarcoidosis was diagnosed based on the latest American Thoracic Society (ATS), European Respiratory Society (ERS) and World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) criteria.[1] Although these guidelines were published only in 1999, we verified that all patients included in the present study fulfilled all designated criteria. Patients displaying evidence of mycobacterial or fungal infection and those with a history of ingestion of drugs or agents causing granulomatous lung disease were excluded. Data included patient demographics, symptoms, details of co-morbid illnesses, sarcoidosis stage, treatment, pulmonary function and CT findings.

The modified Scadding[9] classification system was applied to stage chest radiography (CXR) findings and patients were grouped as Stage 0 (no radiographic abnormality), Stage 1 (bilateral hilar adenopathy with no parenchymal abnormality), Stage 2 (bilateral hilar adenopathy with interstitial parenchymal infiltrates), Stage 3 (interstitial parenchymal infiltrates without hilar adenopathy) and Stage 4 (pulmonary fibrosis). CT reports collected from medical records were assessed for the presence of the following recognized CT patterns:[10] (1) mediastinal and/or hilar lymph node enlargement, (2) ground-glass opacity, (3) consolidation, (4) nodules <3 cm in diameter, (5) thickening of bronchovascular bundles, (6) linear opacity including interlobular septal lines and interstitial thickening, (7) bronchial narrowing secondary to lymph node compression, (8) bullae, (9) and features indicating scarring and fibrosis (grouped together) that included the following: traction bronchiectasis, honeycombing, cysts, and/or volume loss. All CT scans were performed within 1 to 10 years after diagnosis (n=67). Extrapulmonary organ involvement was described according to the criteria established by Judson and colleagues.[11] Treatment was defined as a requirement for corticosteroids with or without immunosuppressive therapy within 3 months of data collection. Treatment regimens applied were grouped as follows: none (no treatment), corticosteroids, corticosteroids and azathioprine, corticosteroids and methotrexate, and oxygen therapy. Treatment decisions were based on individual physician opinions. Disease duration was defined from the time of diagnosis until the last follow-up.

Spirometry was performed and plethysmographic lung volume and single-breath diffusion capacity of carbon monoxide (DLCO) measured. Forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV$_1$), and total lung capacity (TLC), were determined, and values were expressed as percentages of predicted values appropriate for gender, weight and age. Measures of DLCO were made by the single-breath technique and results were corrected for patient hemoglobin level. Calculation of lung volume and measurement of diffusion capacity were performed according to the recommendations of the American Thoracic Society.[12,13] All lung function measurements used in this study were performed within 4 weeks of diagnosis (n=94 for FVC and FEV$_1$; n=75 for TLC; and n=50 for DLCO).

Data were entered into MS Excel and analyzed using the statistical Software Package for the Social Sciences (SPSS pc+ Version 13.0; SPSS Inc, Chicago, IL). Descriptive statistics (mean, standard deviation and percentage) were applied to summarize quantitative and qualitative variables. The chi-square test was used to compare the proportion of qualitative variables. A *P* value <.05 was considered statistically significant.

RESULTS

Our study cohort included 84 native Saudi (80.8%) patients and 20 (19.2%) patients of other Arab origins. The female-to-male ratio was 1.8:1 (Table 1). Mean (SD) age at diagnosis was 46.9 (12.5) years. Females tended to be older than males at the time of diagnosis 50.1 (13.8) *vs*. 48.1 (14.6) years (*P*=.5). The majority of patients (77%) were 40 years or older at diagnosis (Figure 1), and females in this category significantly outnumbered male patients (66.3% vs. 33.7%, *P*=.003). At the time of initial visit, the mean symptom duration was 8 months, with dyspnea as the most common complaint. The mean follow-up duration from the date of diagnosis was 5.4 years.

The procedures performed to obtain diagnostic histological specimens included bronchoscopy (trans-

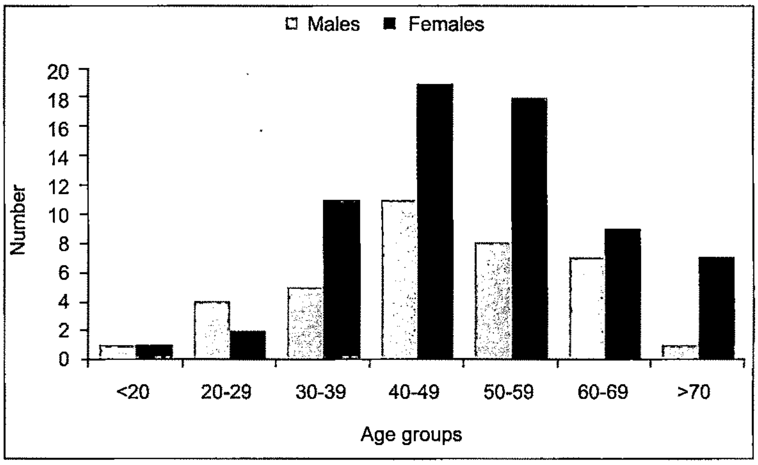

Figure 1. Frequency distribution of sarcoidosis by age group (males vs. females).

Table 1. Demographic and clinical characteristics of patients with sarcoidosis.

Variables	Mean	Standard Deviation	No. (%)
Age (years)	46.9	12.5	
Gender			
Males			37 (35.6)
Females			67 (64.4)
Male: Female ratio			1: 1.8
Smoker			16 (15.4)
Non-smoker			88 (84.6)
Presenting symptoms			
Dyspnea			79 (76.0)
Cough			75 (72.1)
Weight loss			34 (32.7)
Co-morbid illnesses			
Diabetes mellitus			33 (31.7)
Hypertension			26 (25.0)
Ischemic heart disease			7 (6.7)
Chest radiographic stage			
Stage 0			6 (5.8)
Stage I			24 (23.1)
Stage II			44 (42.3)
Stage III			17 (16.3)
Stage IV			13 (12.5)
Extra-pulmonary organ involvement			
Eye			10 (9.6)
Liver, spleen			9 (8.6)
Skin			4 (3.8)
Bone			3 (2.9)
Kidneys			2 (1.9)
Hypercalcemia			8 (7.9)
Other*			3 (2.9)
Treatment			
None			32 (30.8)
Corticosteroids			54 (52)
Corticosteroids + Azathioprine			8 (7.7)
Corticosteroids + Methotrexate			7 (6.7)
Oxygen therapy			3 (2.9)

*Central nervous system, n=1; heart, n=1; muscle, n=1

bronchial [TBB] or bronchial biopsy) in 57 patients (54.8%), mediastinoscopy in 14 (13.5%), surgical lung biopsy in 10 (9.6%), and other biopsies (peripheral lymph node, liver, skin, or renal) in 23 (22.1%) patients. The majority of patients displayed impairment in lung function parameters at presentation. The mean (SD) for FVC, FEV_1, TLC, and DLCO as percentages of predicted values were 74.7 (22.4), 74.5 (21.6), 78.1(18.9) and 61.9 (19.7), respectively. Significant impairment in FVC of <50% was present in only 17% of patients. Approximately two-thirds of patients continued to receive corticosteroids and/or immunosuppressive medication following examination of their previous medical records.

The most frequent CT patterns observed were mediastinal lymph node enlargement in 49 (73.1%) patients (Table 2). Parenchymal abnormalities indicating fibrosis were noted in 31 patients (46.3%) and the most common fibrotic pattern was traction bronchiectasis. Four patients died during the study period mean follow-up 5.4 years, including three females. In all cases, death was attributed to respiratory failure.

DISCUSSION

Sarcoidosis affects individuals worldwide, and shows a predilection for adults less than 40 years of age.[1] However, several investigators have identified older patients, with women tending to be of greater age than men.[4,14] In the large "case control etiologic study of sarcoidosis" (ACCESS) study involving several geographic regions of the United States, women patients were generally older than men and one-third of patients were 60 years of age or over.[2] In the present analysis, mean patient age at diagnosis was 49.3 years, consistent with earlier reports on Arab patients with sarcoidosis.[6,8]

A bimodal incidence peak, mostly in women, has been described in Nordic countries and Japan, with the second peak occurring at an average age of 50 years or older.[4,14] In our study, the peak occurred at 41-50 years of age in males and 41-60 years in females, with a higher proportion of women patients above the age of 70 years. Limited reports appearing to date have described sarcoidosis among elderly patients.[15-17] In an earlier study, Chevalet and colleagues reviewed 30 elderly patients (21 women and 9 men) above 70 years of age (mean age, 74 years) diagnosed with sarcoidosis.[15] Whereas alterations in general health were the major diagnostic sign, overall prognosis was similar to that in young subjects. Interestingly, in our cohort, the mean age of elderly patients diagnosed after 70 years of age was higher at 79.6 years (73-90 years), with a preponderance of women. Intrathoracic involvement; along with symptoms of cough and dyspnea, were the predominant findings. As elderly patients additionally present with characteristic symptoms of pulmonary and multisystem disease, sarcoidosis should be considered in the differential diagnosis of these disorders.

In the current cohort, 64.4% patients were women, consistent with previous studies including reports on Arab patients with sarcoidosis, disclosing a higher disease rate in women compared to men.[4-6,8] Pulmonary manifestations are typically predominant, but virtually any organ system can be involved.[1] The coughing frequency at the time of diagnosis varies among regions, from 3% of patients in Japan[5] to 100% in another series.[18] Moreover, the mode of presentation differs between countries. For instance, Japanese patients are more likely to present with ocular symptoms, whereas respiratory symptoms and erythema nodosum are the common clinical presentations in Finland.[5] In our patients, dyspnea and cough were the most common complaints, in keeping with previous reports on sarcoidosis in Arab populations.[6,8]

The prevalence and distribution of extrapulmonary involvement varies worldwide. These variations can be explained by varying degrees of susceptibility according to race and ethnicity, and are probably related to moderation of the effects of genetic background. The rate of extrapulmonary involvement ranged from 1% to 9.6% in our patient population, depending on the organ involved. However, we believe that our data, along with those of earlier studies focusing on Middle Eastern populations,[6,8] do not represent an accurate estimation of extrapulmonary organ involvement, that would permit meaningful comparison with findings reported elsewhere, because our patients were recruited from pulmonary clinics. Consequently, individuals presenting to other specialists would not have come to our attention.

Chest radiographic findings appear to vary worldwide. For example, higher chest radiographic stages are detected among Finnish patients, whereas Japanese patients are more likely to present with Stage I disease.[5] In our study, 42.3% of the cohort presented with Stage II disease, in keeping with other reports on Middle Eastern patients with sarcoidosis.[6-8] At the time of diagnosis, the percentage of sarcoidosis patients diagnosed with radiographic Stage 0 varied significantly (5.7% in the current study, 1% in Finnish patients, and 19% in Japanese patients).[5] The number of patients with radiographic Stage IV disease was higher in the present study (12.5%) compared to what was reported by Behbehani and colleagues (1.8%).[6] Thus, race and/or ethnicity may contribute to susceptibility to sarcoidosis and disease severity.

Table 2. CT findings in 67 patients with pulmonary sarcoidosis.

CT scan features	n	%
Mediastinal lymph node enlargement	49	73.1
Hilar lymph node enlargement		
Unilateral	8	11.9
Bilateral	28	41.8
Nodules	36	53.7
Traction bronchiectasis	24	35.8
Ground glass opacities	22	32.8
Thickening of bronchovascular bundles	15	22.4
Interlobar lines	12	17.9
Cysts	9	13.4
Septal lines	8	11.9
Honeycombing	7	10.4
Consolidations	4	6.0
Bronchial narrowing secondary to lymph node compression	4	6.0
Bullae	1	1.5

Aberrations in pulmonary function tests (PFTs) are common in patients with sarcoidosis, with abnormalities detected in 20% of patients with Stage 1 disease and in 40% to more than 70% of patients with Stage 2, 3, or 4 disease.[1] The majority of our cohort exhibited abnormalities in PFTs, with 17% of patients displaying markedly reduced FVC, <50% of normal, at presentation. Given the limited predictive value of baseline PFTs[19-24] and the variable natural history of the disease, other outcome measures that provide better objective information, and thus afford a more accurate predictive model for morbidity and mortality, are essential.

Several studies have investigated the role of CT, including high resolution CT (HRCT), in sarcoidosis patients.[25-30] However, routine CT scanning is not advocated in management of sarcoidosis except in patients in whom normal or atypical chest radiography is evident, or specific complications are suspected, such as in patients with pulmonary fibrosis, bronchiectasis, aspergilloma, or malignancy.[1,31] In the present study, mediastinal lymph node enlargement was the most common CT finding, in keeping with previous reports on patients with pulmonary sarcoidosis.[25,28] Correlation of HRCT findings with pulmonary function studies has been variable, probably related to interstitial vs. bronchial involvement, or reflecting different HRCT scoring applied in various reports.[27-29] In our current study we did not attempt to determine such relationships, as CT scans were not obtained systematically, and were not performed simultaneously with PFT evaluation. Abehsera and associates[30] evaluated chest CT scans of sarcoid patients who displayed chest radiographic evidence of fibrotic changes (Stage IV disease), and found the following three different CT patterns: bronchial distortion including traction bronchiectasis (predominantly central in nature), honeycombing (predominantly peripheral and often in the upper zones), and a linear pattern (predominantly diffuse in nature). These patterns were recognized in 47%, 29%, and 24% of patients, respectively. Notably, almost half of our patients had developed pulmonary fibrosis based on CT, where traction bronchiectasis was the most frequent CT pattern found, consistent with data of a previous study.[30] Identification of prognostic variables based on HRCT patterns has also produced discordant results,[27,30,32,33] probably related to differences in the methodology used in various studies or (perhaps more likely) related to disease expression moderated by gene-environmental interaction. Further large-scale studies are warranted to explore such effects within the Arab population.

Our study had several limitations. First, this was a retrospective review, and several values, such as TLC and DLCO, were not available for all patients. Second, there was a selection bias, because the study was performed in tertiary hospitals, in which patients with severe complaints and in advanced stages of sarcoidosis were more likely to be referred.

In conclusion, a significant number of this sample of Arab patients diagnosed with pulmonary sarcoidosis were symptomatic and displayed impairment in lung function parameters at presentation. Mediastinal lymphadenopathy was the most frequent CT finding and a significant number of patients progressed to pulmonary fibrosis.

Future studies need to focus on disease prevalence and patterns preceding development of lung fibrosis attributable to sarcoidosis.

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Management of end-stage heart failure: a perspective on the Arab Gulf states

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Ann Saudi Med 2009; 29(6): 460-466
PMID: 19847084 DOI: 10.4103/0256-4947.57169

The ever expanding epidemic of end-stage heart failure represents one of the greatest challenges of modern cardiovascular medicine. With medical treatments hampered by significant limitations, physicians caring for patients with advanced heart disease have turned to cardiac transplantation and durable mechanical circulatory assist devices as definitive therapies. These advanced therapeutic modalities are not widely available outside the United States and Europe, but nevertheless offer enormous potential for patients in the Arab Gulf suffering from end-stage heart failure. This review will discuss the management of end-stage heart failure in the Gulf States, with an emphasis on therapies best utilized within a framework of regional cooperation and coordination.

The management of patients with end-stage heart failure has emerged as one of the major challenges in cardiovascular medicine. There has been considerable progress in the understanding of heart failure pathophysiology leading to medical therapies that impact the prognosis and symptoms of chronic heart failure.[1-4] Therapeutic options for end-stage failure, however, remain limited and include intravenous inotrope therapy, heart transplantation, or mechanical circulatory support.[5,6] These advanced therapeutic modalities are available at select centers in the United States and Europe, but are not routinely considered in other global regions. The Arab Gulf is one such region. The primary barriers to widespread adoption of these advanced treatments are limited financial resources, lack of medical expertise, and cultural attitudes about organ procurement. The Arab Gulf is united by a common religion and culture and has a rapidly expanding medical expertise and proficiency. This review will discuss the management of end-stage heart failure in the Gulf States, with an emphasis on therapies that might be organized across national boundaries and closely coordinated by the Gulf's emerging tertiary care centers.

Incidence of heart failure

The incidence of cardiovascular disease and heart failure is projected to increase substantially in the Arab Gulf States as the region completes an epidemiological transition fueled by socioeconomic change.[7] Even as access to health technology increases, trends in urbanization, inactivity and receding infectious pandemics are allowing cardiovascular diseases to become the leading cause of morbidity and mortality. Hypertension is now estimated to affect more than one fourth of the Saudi population.[8] The traditional high fiber, low fat diet has been replaced by a Western diet higher in fat. This change in dietary intake along with a more sedentary lifestyle has led to obesity in 35% of Saudi's as defined by a body mass index (BMI) ≥ 30 kg/m^2 and diabetes mellitus in 23.7%.[9-13] With atherosclerotic risk factors on the rise, coronary artery disease and ischemic cardiomyopathy will become more prevalent.[14] Ischemic heart disease is already the leading cause of heart failure in Western Europe and the United States, countries that were the earliest to complete the epidemiologic transition.[15,16] For example, heart failure currently accounts for over $35 billion in health care costs in the United States and remains the leading hospital discharge diagnosis in patients over the age of 65.[17]

It is estimated that 5-10% of heart failure patients have end-stage, refractory disease.[18] These patients suffer from extreme exercise intolerance, debilitating dyspnea, often even at rest, and poor quality of life. The aggregate five-year survival rate of patients with heart failure is approximately 50 percent, whereas the one-year mortality rate of those with advanced disease may exceed 50 percent.[19,20] This one-year mortality rate for New York Heart Association (NYHA) functional class IV heart failure exceeds that of HIV/AIDS and common malignancies, including breast, lung, and colon cancer.[17] Caring for patients with the most advanced heart failure consumes over 60% of all health-care expenditures for patients with heart failure.[21] This economic burden on the health care system is a consequence of frequent hospitalizations and the use of costly device therapies such as biventricular pacemakers and the implantable cardioverter defibrillators (ICDs).[22-26] Heart failure patients are now less likely to suffer sudden cardiac death as a result of widespread use of neurohormonal antagonists and ICDs.[27,28] These therapies have prolonged survival with heart failure leading to a larger proportion of patients in the later stages of this progressive disease who suffer the hemodynamic consequences of refractory fluid congestion and end-organ underperfusion. The increasing prevalence and severity of heart failure combined with the very poor quality of life and dismal prognosis mandate that other therapies be considered for heart failure patients living in of the Arab Gulf States.

Medical therapies for advanced heart failure

The major advances in heart failure therapies have been primarily seen with systolic heart failure with a reduced ejection fraction. There is no debate that beta-adrenergic blockers, angiotensin converting enzyme (ACE) inhibitors, and angiotensin-receptor blockers (ARBs) offer an improved survival, and the frequency of their administration is emerging as a quality of care benchmark.[29-34] Aldosterone antagonists have a clear role in post-infarction patients and symptomatic heart failure, although serum potassium and renal function must be carefully monitored.[35-38] Hydralazine and nitrates continue to have a time-honored place in heart failure management, especially in those intolerant of ACE-inhibitors or ARBs or persistent renal compromise.[39] Loop diuretic therapy has a central role for symptomatic relief but has not been shown to confer a survival benefit.[1-3] Despite being available since the 18th century, digitalis glycosides such as digoxin reduce hospitalizations for heart failure and provide modest symptomatic relief, but they do not prolonged survival.[40,41]

In patients with diastolic heart failure, the most effective therapies will include diuresis, control of blood pressure, and maintenance of sinus rhythm.[1-3,42] There have been no studies demonstrating a robust mortality benefit of any agent in heart failure with a preserved ejection fraction even though such patients may constitute half of all patients with heart failure.[43,44]

Most medical therapies have been directed toward NYHA Functional Class II-III or AHA/ACC Stage C heart failure and have a limited role once the evolution of heart failure have moved to Class IV NYHA or Stage D (Tables 1 and 2). In fact, one definition of end-stage heart failure is an intolerance to or failure of conventional therapy.

Cardiac resynchronization therapy

Many heart failure patients with a low ejection fraction often also have interventricular conduction delay, as manifest by a widened QRS complex (>120 msec) on electrocardiogram from either a bundle branch block or nonspecific conduction delay. This delay creates dyssynchronous contraction of the left ventricle and can contribute to remodeling, mitral regurgitation and symptoms of congestion.[23] Class III-IV Heart failure patients with reduced ejection fraction and conduction delay (QRS width >120-150 msec) may benefit from cardiac resynchronization therapy (CRT), also known as biventricular pacing.[25] Pacemaker leads are placed in the right ventricular apex and the lateral free wall of the left ventricular via the coronary sinus to "resynchronize" contraction of the left ventricular. This may lead to reverse remodeling, decrease mitral regurgitation and a mortality benefit in select patients.[26,45] Not every patient will respond to CRT. Prospectively identifying responders and nonresponders is an active area of research.

Heart failure management programs

The primary goals in the management of end-stage heart failure are to reduce hospitalizations and to improve quality of life. Disease management programs have been shown to be effective in this regard, providing a structured continuity between the hospital discharge and the home setting.[46,47] Pre-discharge education is central to its success. A team of providers that includes physicians, nurses, nurse practitioners, physicians assistances and pharmicists, working with established guidelines, can provide meaningful interventions when there is frequent communication with outpatients.[48] For example, daily weights can be monitoring to guide adjustments of diuretic dosage and home blood pressure readings can be used to adjust afterload reduction.[49] Implantable technology for daily estimation of left heart filling pressures can provide additional he-

Table 1. New York Heart Association functional class.

Class I – No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea (shortness of breath).

Class II – Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.

Class III – Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea.

Class IV – Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.

Table 2. Stages of heart failure.

Stage A – At risk for heart failure but without structural heart disease or symptoms of heart failure

Stage B – Structural heart disease but without signs of symptoms of heart failure

Stage C – Structural heart disease with prior or current symptoms of heart failure

Stage D – Refractory heart failure requiring specialized interventional (e.g. mechanical circulatory assist devices, intravenous inotropes or vasodilators)

modynamic insights by telemonitoring.[50] Heart failure management programs are most effective when established as part of a larger commitment to advanced heart failure care, including transplant or mechanical support.

Management of end-stage heart failure

Inotropic therapy

Many patients with refractory congestive symptoms and low cardiac output despite conventional therapy will benefit from infusion of a positive inotrope.[51] Most commonly performed as an inpatient strategy, select patients can be transitioned to outpatient therapy infusion therapy once safe administration has been demonstrated.[52] Though intravenous inotropes such as dobutamine (a beta-adrenergic receptor agonist) or milrinone (a phosphodiesterase-3 inhibitor) provide short-term improvements in congestive symptoms and cardiac output, this comes at the price of increased risk of ventricular tachycardia and direct cardiac myocyte toxicity.[53,54] Prophylactic ICD are routinely placed to protect patients on chronic inotropic infusions from malignant tachyarrhythmias.[51] Continuous outpatient inotropic therapy may be administrated through a tunneled central venous catheter and can help to maintain end-organ perfusion in patients awaiting heart transplantation.

Heart transplantation

Orthotopic cardiac transplantation remains the definitive therapy for terminal heart failure.[55] Surgical techniques can be acquired by many tertiary care centers. Recipient criteria have been well-established and immune suppression protocols have been standardized. Long-term post-transplantation care is managed by an integrated team of cardiologists, nurses, nurse practitioners, physicians assistants and pharmacists. After cardiac transplantation patients can achieve an acceptable 5-year survival of 70%, a 10-year survival of 60%, and markedly improved quality of life.[56] Despite these impressive results in select patients, the ultimate potential for cardiac transplantation to stem the tide of the rising heart failure epidemic remains limited. Even in the United States, donor organ availability has remained static even as the waiting list for heart transplant grows.[57-59]

The primary barrier to cardiac transplantation in the Gulf States is the ad hoc organization of donor supply. While a limited number of centers have been able to perform the intermittent transplant, no program in the Gulf has achieved sufficient experience that would meet program certification goals of national regulatory bodies. Saudi Arabia is the only country within the Gulf region with a solid organ transplant organization, the Saudi Center for Organ Transplantation (SCOT), and King Faisal Specialist Hospital in Riyadh is the only heart transplant center. In 2008, the last year for which data is available, there were 19 cardiac transplantations in SCOT, preceded by 12 transplants in the year prior.[60] To put this in perspective, the United States Center for Medicare Services requires advanced heart failure programs to perform 12 transplants per year for 3 years to secure certification. The absence of a well-organized solid organ procurement apparatus in the Gulf States has prevented the expansion of cardiac transplantation as a viable modality of therapy for select end-stage heart failure patients.

Sadly, mortality is rapidly rising in the Gulf states from motor vehicle collisions as well as cerebral vascular accidents from poorly controlled hypertension—the most common conditions causes brain death while preserving the potential for organ donation. While automobile accidents and strokes present a significant challenge to public health authorities, they also represent an opportunity to coordinate donor management, procurement and distribution. The Gulf Cooperative Countries (GCC) have already established political, travel and trade alliances. Established in 1981, the six GCC countries include Saudi Arabia, United Arab Emirates, Kuwait, Oman, Qatar and Bahrain with a population base approaching 41 million and a unifying culture. Organization of solid organ transplantation dovetails with the GCC charter which specifically outlines a goal of integration and interconnection between members states in all fields to encourage cooperation and joint ventures.

Many existing organ procurement organizations cross political boundaries to serve the collective transplant need. In the United States, the New England Organ Bank represents 6 states and Bermuda, with a population base of 11.2 million. The Eurotransplant Interntational Foundation serves the transplant needs of Austria, Belgium, Germany, Luxembourg, the Netherlands, Slovenia and Croatia, with a population of 124.5 million and coordinated 6,600 solid organ donations. In order to address the current and future needs of all solid organ transplantation for the GCC, a coordinated transnational organ procurement organization representing the interests of the populations of all the Gulf States must be considered.

It is beyond the scope of this article to discuss the many religious and cultural issues surrounding solid organ transplantation. Organ donation, harvest and transplantation are a relatively new cultural concept in the Islamic and Arabic world and subject to a variety of interpretations. Renal transplantation, given its longer history, has wider acceptance than other solid organ programs.[61-63] The Islamic medical community may have different interpretations than the general community, and at the present time, many medical centers follow the dictum that organ donation can be religiously rewarded—*And if any one saved a life, it would be as if he saved the life of the whole people. (Al-Maeda, Chapter 5, Verse 32)*[64]

Ventricular assist devices

Given the immediate limitations to cardiac transplantation in the Gulf States and ultimate limitations of donor supply, ventricular assist devices (VAD) may be the most reasonable option for long-term hemodynamic support.[6,65,66] (Tables 3 and 4) VAD technology has rapidly advanced, and such may now be considered as a reasonable therapy for both transplant eligible patients and those excluded due to conventional co-morbidities.[67] VADs provide mechanical circulatory assistance after being placed in parallel to the patient's own heart which is left in its native anatomic position, unlike the total artifical heart or orthotopic transplantation.[68] VADs are broadly categorized as pulsatile pumps or continuous flow rotary devices. Pulsatile assist devices were the first to be developed and the first approved for destination therapy (Heartmate XVE) after the landmark REMATCH trial.[69] New technology includes the axial or continuous flow devices.[70] These next generation VADs have a lower profile, making them easier to implant even in smaller patients, and, offer quiet, vibration free operation. These continuous flow pumps may also be easier to manage by the patient and their family, and seem to have extended durability compared to the pulsatile technology. By late 2008, there was evidence that the axial flow technologies were emerging as superior technology to the pulsatile devices, and it is anticipated that they might be the technology of choice in the near future. Each of these devices can be managed in the outpatient setting and permit full ambulatory capability.

The clear survival advantage and quality of life for patients receiving VADs compared to medical therapy now justifies their use for circulatory support well beyond the transplant setting. In REMATCH, the implantation of a left-sided VAD was associated with a relative reduction in the risk of death of 48 percent during the entire follow-up period of 4 years and an absolute reduction in the mortality rate of 27 percent at one year.[69,71] Quality of life with a VAD is substantially better than that experienced by patients just before VAD support. Many patients move from NYHA Class IV to Class I-II. These results portend an acceptable quality of life for the long-term use of VADs as an alternative to medical therapy for patients in need of cardiac transplantation but who will not receive it.[72]

Prior to VAD implantation, all patients should be evaluated at cardiac centers with specific expertise in advanced heart failure.[73] Oftentimes patients benefit from more aggressive and expert management of their

Table 3. Indications for ventricular assist device implantation.

NYHA functional class IV symptoms
Life expectancy <2 years
Not a heart transplantation candidate
Failure to respond to optimal medical management for 60 of the last 90 days
Left ventricular ejection fraction ≤25%
Refractory cardiogenic shock or cardiac failure[‡]
Peak oxygen consumption ≤12 ml/kg/min with cardiac limitation
Continued need for intravenous inotropic therapy limited by symptomatic hypotension, decreasing renal function or worsening pulmonary congestion
Recurrent symptomatic sustained ventricular tachycardia or ventricular fibrillation in the presence of an untreatable arrhythmogenic pathologic substrate
Body surface area >1.5 m^{2}[±]

NYHA: New York Heart Association; [‡]Cardiogenic shock may be seen following acute myocardial infarction or cardiac surgery; Implantation should only be considered in patients without potential for recovery; [±]Smaller individuals may be fitted with available paracorporeal, small-sized pulsatile or newer axial-flow devices.

heart failure, including a restructuring of their medical regimen.[74] If symptoms remain refractory to standard therapy, patients may be considered for VAD implanatation in one of three categories: 1) "Bridge to Recovery" for patients who are not expected to need long term support; 2) "Bridge to Transplantation" for patients suitable for cardiac transplant but who are too ill to wait until an organ becomes available; 3) "Destination Therapy" for patients needing long-term support but who are ineligible for cardiac transplantation by conventional criteria.[75] The distinction between "bridge to transplant" and bridge to destination" may be too arbitrary. There will be inevitable "bridge to transplant" patients that develop complications precluding successful transplant, and there will be inevitable "bridge to destination" patients who improve sufficiently to be able to be transplanted without complication. Hence, "bridge to decision" is perhaps a more honest representation of options to many patients and their families.

Table 4. Contraindications to ventricular assist device implantation.

Relative contraindications
Age>65 years, unless minimal or no other clinical risk factors
Chronic kidney disease with serum creatinine level >3.0 mg/dL
Severe chronic malnutrition (BMI<21 kg/m^2 in males and <19 kg/m^2 in females)
Morbid obesity (BMI>40 kg/m^2)
Mechanical ventilation
Severe mitral stenosis, moderate to severe aortic insufficiency, or uncorrectable mitral regurgitation
Absolute contraindications
Reversible, transient causes of heart failure
Recent or evolving stroke
Neurologic deficits impairing the ability to manage device
Coexisting terminal condition (e.g., metastatic cancer, cirrhosis)
Abdominal aortic aneurysm ≥5 cm
Biventricular failure in patients older than 65 years
Active systemic infection or major chronic risk for infection
Fixed pulmonary or portal hypertension
Severe pulmonary dysfunction (e.g., FEV_1<1 liter)
Impending renal or hepatic failure
Multiple organ system failure
Inability to tolerate anticoagulation
Heparin induced thrombocytopenia
Significant underlying psychiatric illness or lack of social support that may impair ability to maintain and operate VAD

BMI: body mass index; COPD: chronic obstructive pulmonary disease; FEV_1: forced expiratory volume in 1 second. Adapted from Wilson, et al.[81]

The ample costs associated with VAD implantation are contingent on the type of device used, length of hospital stay, country-specific health economics, and the nature of the underlying disease.[76-78] The mean total costs for VAD implantation is US $210 132 over an average period of 9.5 months.[79] This does not meet current thresholds for cost-effectiveness, as expensive technologies can be cost effective while inexpensive ones can be cost ineffective. In the Gulf States, most of the health expenses are carried by the central governments and providing such expensive therapy may be considered a burden unless proven cost-effective. The ultimate comparison will balance the costs of treating heart failure with the incalculable costs of death and disability.

Any cost-effectiveness analysis must also take into account the rapid evolution of technology used. Since the axial flow devices are smaller, simpler to use, and more durable, it can be anticipated that they will also be more cost effective. In addition, the cost of a new medical technology usually declines as it becomes more widespread and management issues standardized. Continued improvements to the next generation of devices can be anticipated to extend durability and reduce complication rates.[80]

Conclusions

The management of heart failure is both a challenge and an opportunity for the health care systems of the Gulf region. Advanced therapies for terminal heart failure remain elusive. While cardiac transplantation remains a potential option, there are logistical limitations in the Arabic world at the present time that limit widespread applicability. The new technologies of mechanical circulatory assistance may be a better option for end-stage patients, and requires thoughtful analysis and candid discussion about the priorities of health care resource allocation. Heart failure patients in the Gulf are deserving of these advanced therapies that will improve the quality and length of their lives.

Acknowledgment

This research is supported by a scholarship to Dr. Al Habeeb by the King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia.

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brief report

The prevalence and diagnostic performance of anti-cyclic citrullinated peptide antibody in rheumatoid arthritis: the predictive and discriminative ability of serum antibody level in recognizing rheumatoid arthritis

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Ann Saudi Med 2009; 29(6): 467-470

PMID: 19847085 DOI: 10.4103/0256-4947.57170

BACKGROUND AND OBJECTIVES: The utility of anticyclic citrullinated peptide (anti-CCP) antibody in the diagnosis of rheumatoid arthritis (RA) varies across different studies. We determined the diagnostic performance and predictive ability of anti-CCP for RA.

METHODS: We studied 201 patients with RA and compared them with 208 non-RA patients as controls. RA patients included in the study fulfilled the American College of Rheumatology revised criteria and patients with other diseases as well as those with undifferentiated arthritis (UIA) were used as controls. Anti-CCP was measured by enzyme-linked immunosorbent assay (ELISA) and rheumatoid factor (RF) by the agglutination method. The optimal cutoff value and diagnostic accuracy were determined using receiver operating characteristics (ROC) curve and area under the curve (AUC).The sensitivity and specificity were determined by comparison of RA patients with non-RA controls.

RESULTS: The anti-CCP test was positive in 164 patients with RA for a sensitivity of 81.6%, specificity of 87.5%, and overall accuracy of 84.6%. The respective values for RF were 75.6%, 86.5% and 84.4%. The anti-CCP test discriminated RA from non-RA patients with high accuracy (AUC=0.889 [0.017] 95% CI, 0.856-0.952, *P*=.001), and predicted progression of UIA to RA with moderate accuracy (AUC=0.733 [0.069], 95% CI 0.60-0.87, *P*<.006) at a sensitivity of 75% and a specificity of 68.1%. Among 60 UIA patients, in 16 (26.7%) who differentiated to RA, the mean (standard deviation) for anti-CCP was significantly higher than in 24 (40%) patients who progressed to non-RA (134.8 [172] vs 46 [86] U/mL, *P*<.01).

CONCLUSION: These findings indicate that anti-CCP yields higher sensitivity and overall accuracy, but slightly greater specificity than RF for diagnosis of RA. Anti-CCP positivity, particularly a higher level of serum antibody in patients with UIA, may be a predictor of subsequent RA.

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease with a progressive course that may lead to joint destruction and subsequent disability if not effectively treated.[1] Early diagnosis and treatment may prevent joint destruction and suppress disease progression.[2]

At present, the diagnosis of RA is based on the American College of Rheumatology (ACR) revised criteria, which include IgM rheumatoid factor (RF), and clinical and radiological criteria.[3] However, RF positivity is nonspecific for RA, because it can be detected in other non-RA diseases as well as in healthy individuals. The initial diagnosis of RA at the initial period can be difficult in some cases due to lack of typical symptoms and signs to fulfill the ACR criteria. Therefore, the presence of a sensitive and specific test for diagnosis of RA at an early stage would be very useful for initiating treatment as well as in discriminating RA from non-RA diseases. Among the several autoantibodies described for diagnosis of RA, anticyclic citrullinated peptide (anti-CCP) antibodies yielded a higher specificity with comparable or even higher sensitivity compared with RF.[4-8]

Anti-CCP antibodies are produced locally at sites of inflammation, not only in the synovium of RA, but also in other non-RA diseases.[9] Therefore, anti-CCP positivity may be expected in a proportion of patients with non-RA diseases as well. Hence, discrepancy in sensitivity and specificity of anti-CCP between various studies may be attributed to differences in false-positive rates among selected controls. However, other factors such as detection techniques and genetic background may be also responsible for these variations. For this reason, the present study was designed to determine the diagnostic performance of anti-CCP in patients who presented to an outpatient medical clinic in Babol, Iran.

METHODS

All patients were selected consecutively over a 1-year period from among patients visiting rheumatology clinics in Babol, Iran. Patients with inflammatory arthritides who had one or more inflamed joints were included in this study. The study was approved by the ethical committee of Babol University of Medical Sciences. RA patients included in the study fulfilled the ACR revised criteria; non-RA patients considered as controls fulfilling other criteria for other non-RA rheumatic diseases.

A medical history and complete clinical, laboratory and radiological examination were performed on all patients. Initially, 185 patients diagnosed as having RA and 50 were non-RA. Sixty patients with a mean (SD) disease duration of 2.3 (3.1) years, who did not fulfill any diagnostic criteria, were classified as having undifferentiated inflammatory arthritis (UIA).

All patients were treated appropriately and followed for at least 1 year or longer. Patients visited every 2 to 3 months. The initial diagnoses were reviewed or changed when there were new clinical, laboratory, or radiological findings. Final diagnoses of RA or non-RA, which were made at the latest visit, were considered in the statistical analysis.

Table 1. Frequency of patients with rheumatoid arthritis and other rheumatic diseases at presentation and over the follow-up period.

Diagnosis	No. of patients	
	Initial diagnosis	Final diagnosis
RA	185	201
UIA	60	18
Non-RA inflammatory arthritis	50	76
Healthy controls	114	114
Total	**409**	**409**

Serum samples were obtained for assessment of anti-CCP and RF. Anti-CCP levels were determined by ELISA using the Euroimmune kit, which measures human IgG antibody against anti-CCP. RF was assessed by the latex agglutination method. Additionally, sera from 114 apparently healthy subjects without arthritis were tested to assess the specificity of anti-CCP and RF.

Receiver operating characteristics (ROC) analysis was applied by plotting sensitivity against 1-specificity for various cutoff points of anti-CCP. The optimal cutoff value that best distinguished RA from non-RA was determined at the maximum value of Youden's index, which was estimated by sensitivity + 1-specificity.[10] The overall diagnostic accuracy and predictive ability were estimated based on the area under the curve (AUC) which is reported with its standard error.

Considering clinical and radiographic criteria as the gold standard diagnostic test, the diagnostic characteristics were determined by comparison of RA with non-RA controls. Controls consisted of patients with non-RA inflammatory arthritides and 114 subjects who attended the same clinic and were selected consecutively among those without any skeletal diseases. The misclassification rate (MR) was calculated by false negative + false positive divided by the total of the tests performed. Accuracy was calculated by 1−MR and likelihood ratio was calculated by sensitivity divided by 1−specificity.

RESULTS

Two hundred ninety-five patients entered the study (Table 1). After a median follow up of 14 months (range 1-50), 16 of 60 UIA patients met the ACR criteria for RA, 8 patients progressed to SLE, and 18 patients progressed to rheumatic diseases other than RA. In the remaining 18 patients, the diagnosis did not change. The study included 201 RA patients (80% females) with mean age of 51 (14) years with a mean disease duration of 6.6 (6.3) years, 94 non-RA patients with a mean disease duration of 2.6 (4) years and 114 subjects without arthritis with mean age of 39 (16) years who served as controls.

Based on the results of ROC analysis, a serum anti-CCP of 14.8 U/mL yielded the highest Youden's index value for diagnosis of RA at a sensitivity of 81.6%, a specificity of 87.5%, and overall accuracy rate of 84.6% (Figure 1). At this level the anti-CCP test demonstrated a false positive rate of 12.5%, a false negative rate of 18.4%, a misclassification rate of 15.4% and

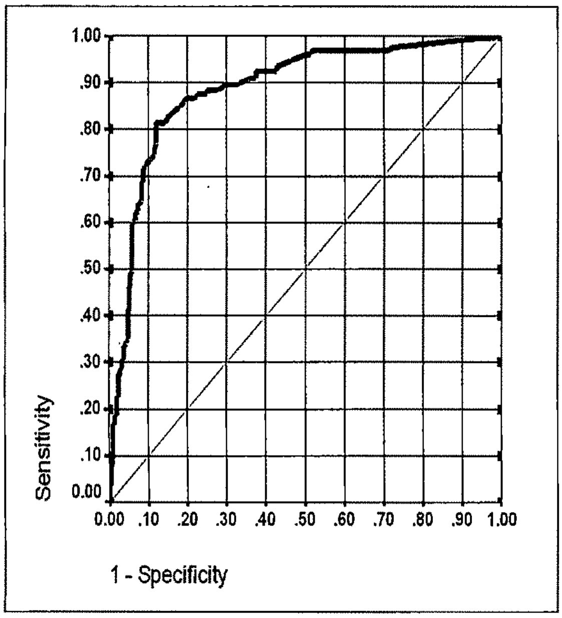

Figure 1. Receiver operating characteristics curve for anti-CCP antibody in the diagnosis of RA.

a positive likelihood ratio of 6.52. Anti-CCP diagnosed RA and differentiated RA from non-RA with high diagnostic accuracy with an AUC value of 0.889 (0.017) (95% CI, 0.856-0.952, P=.001). Patients with initial UIA who subsequently progressed to RA or non-RA were differentiated by anti-CCP at a sensitivity of 75% and a specificity of 68.1% with a moderate accuracy at AUC of 0.733 (0.069) (95% CI 0.60-0.87, P<.006). Anti-CCP was positive in 32 (65.3%) seronegative RA patients. Diagnostic characteristics of anti-CCP and RF are presented in Table 2.

The mean (SD) antibody levels in anti-CCP-positive RA, SLE, and palindromic arthritis, patients were 139 (118), 121 (157), and 130 (94) U/mL, respectively, but the mean anti-CCP in 16 patients with UIA who progressed to RA was significantly higher than in the 24 UIA patients who progressed to non-RA (135 [172] U/mL vs. 46 [86] U/mL, P=.011). RA development in anti-CCP-positive UIA was 6.5 times higher than anti-CCP-negative UIA (46.1% vs. 11.7%, P<.002).

DISCUSSION

We estimated the diagnostic performance and overall accuracy of anti-CCP, and explored the relationship between serum antibody level and progression of arthritis to RA. The results of this study suggest that anti-CCP is a better diagnostic tool than RF for diagnosis of RA with higher sensitivity, only a slightly greater specificity, but a higher diagnostic accuracy. The presence of both antibodies in the serum compared with anti-CCP alone increases the specificity, but decreases both sensitivity and overall accuracy. Moreover, anti-CCP displays a high diagnostic accuracy in discriminating RA from non-RA patients and a moderate accuracy in predicting progression of UIA to RA.

Available data indicate variations in sensitivity and specificity of anti-CCP across different studies.[4,8] Based on a meta-analysis of 37 studies of anti-CCP antibody and 50 studies of RF by Nishimura et al, anti-CCP was more specific than RF for diagnosing RA. The pooled sensitivity, specificity, and positive likelihood ratio for anti-CCP antibody were 67%, 95%, and 12.46, and for IgM RF the values were 69%, 85%, and 4.86, respectively.[11] Among several factors that could explain the discordant sensitivity and specificity between diverse studies, the frequency of a false positive test in non-RA controls deserves further consideration because the specificity is inversely related to the proportion of positive tests among controls. The lower specificity of anti-CCP in the present study compared with other studies can be explained by the presence of a high proportion of false positive non-RA arthritis among controls. In contrast, in studies in which healthy subjects or noninflammatory arthritis patients were selected as controls, the specificity was higher because the likelihood of anti-CCP positivity in healthy subjects or noninflammatory arthritis is lower than in patients with inflammatory arthritides.[6-8]

In another study from Iran of 136 RA patients with a disease duration of less than two years, the sensitivity and specificity of anti-CCP were 62.5% and 89.1%, respectively.[5]

In the present study, not only the presence of anti-

Table 2. Diagnostic characteristics of anti-CCP and rheumatoid factor for diagnosis of rheumatoid arthritis.

Diagnostic tests	Sensitivity	Specificity	Misclassification	Accuracy	Likelihood ratio
Anti-CCP	81.6	87.5	15.4	84.6	6.52
RF	75.6	86.5	18.8	81.2	5.6
Anti-CCP and RF	65.6	95.2	19.3	80.5	13.6

anti-CCP=anticyclic citrullinated peptide antibody; RF=rheumatoid factor

CCP in the serum, but the level of antibody in the serum, was also associated with subsequent progression of UIA to RA. As yet, the relationship between the level of serum antibody and progression to RA was shown only in one previous study.[12] The results of our study confirm previous results, provide further data, and extend evidence-based knowledge. Based on the results of the present study, patients with anti-CCP-positive inflammatory arthritis and patients with a high level of serum antibody, in particular, may progress to RA afterwards.

A important point that could be seen as affecting the interpretation of this study is that palindromic arthritis is considered a risk factor for RA and anti-CCP-positive SLE may develop clinical features similar to RA. Therefore, in a number of anti-CCP-positive non-RA patients, differentiation to RA with subsequent changes in sensitivity and specificity is possible.[13,14] However, the overall results would not be affected significantly.

In conlusion, in Iranian patients, anti-CCP compared to RF yields a higher sensitivity with slightly greater specificity, but higher overall accuracy for diagnosis of RA. Anti-CCP differentiates RA from non-RA with high accuracy. Anti-CCP positivity, particularly a higher level of serum antibody, may predict progression of UIA to RA. Further studies are required to confirm the accuracy as well as the predictive ability of serum antibody level for subsequent RA.

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case report

Diffuse idiopathic hyperplasia of the sternocleidomastoid muscle in a child

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Ann Saudi Med 2009;29(6): 471-473

PMID: 19847086 DOI: 10.4103/0256-4947.57171

Unilateral diffuse or localized enlargement of the sternocleidomastoid muscle (SCM) is an event commonly seen in infancy, and is popularly known as 'sternocleidomastoid tumor'. The condition, which usually spontaneously resolves with or without physiotherapy, is due to a hematoma following a difficult labor. The muscle regains its elasticity and complete function. In some infants it resolves with fibromatous changes in the muscle leading to shortening, fibrosis and finally culminating in torticollis. We describe a case of idiopathic diffuse enlargement of unilateral SCM in a 12-year-old child without any functional compromise or torticollis. The histopathological and clinical characteristics differentiating it from more commonly described sternocleidomastoid tumor or fibromatosis coli are described. We believe this is the first case report of idiopathic hyperplasia of SCM.

Sternocleidomastoid swelling is commonly encountered in infancy as 'fibromatosis coli' or 'immature infantile tumor' following a hematoma due to difficult labor.[1] We report a case of spontaneous unilateral diffuse enlargement of the left sternocleidomastoid muscle (SCM) giving rise to progressive neck swelling in a 12-year-old child. We discuss the unique clinical and histopathological characteristics of this swelling, which can be classified as idiopathic hyperplasia of the SCM.

CASE

A 12-year-old healthy boy presented with spontaneously developed progressive painless swelling of the left sternocleidomastoid muscle in the neck extending linearly from the mastoid process to the sternoclavicular joint along the of same side for 3 years (Figures 1a and 1b). The clavicular head of the muscle did not share the hypertrophy. There were no associated symptoms of fever, restriction of neck movement or weight loss. Workup at another center revealed a fusiform hypoechoic mass along the left SCM on ultrasonography. MRI scan revealed a 12×5×4 cm diffuse hypointense mass on T1-weighted image replacing the left SCM, which was mildly hyperintense on T2 and showed enhancement on IV contrast (Figure 2). There was no enlargement of the cervical lymph nodes or perimysial extension. The parotid, submandibular and thyroid gland appeared normal. Fine needle aspiration biopsy revealed skeletal muscle with degenerative and reactive cellular changes, possibly myositis. Incisional biopsy also reported the histopathology to be consistent with focal myositis (pseudotumor). At presentation to our hospital, the swelling had increased to a size of 15×6×5 cm^3. There was no associated restriction of neck movements or torticollis. On palpation the entire swelling was firm, and nontender with overlying normal skin and no fixation to underlying structures. The forced contraction maneuver for left SCM would make the swelling taut. There was no significant cervical lymphadenopathy.

Due to the progressive increase in size over the previous 3 years, as well as cosmetic issues and the unexplained pathology, the father sought surgical advice and agreed to excision of the left sternocleidomastoid swelling under general anaesthesia. A diagnostic and therapeutic excision of the swollen SCM was carried out through a lateral collar incision overlying the most prominent part of the swelling. Histopathological examination of the specimen revealed skeletal muscle hyperplasia with focal interstitial predominantly chronic inflammatory cellular infiltrate (Figure 3), focal endomysial connective tissue proliferation and a fibroblastic reaction together with degenerative and reactive skeletal muscle fiber changes. No atypia was detected. The histopathological diagnosis was that of a nonspecific proliferative myositis of the muscle.

The child had regular follow-up to observe for any future changes in the contralateral SCM or other neck muscles. At 1-year follow-up he remained well without any recurrence or deformity (Figures 1c and 1d). The child compensated for neck movement by using strap muscles and anterior fibers of the trapezious muscle

DISCUSSION

Unilateral swelling in the neck of a child evokes a list of differentials, including cervical lymphadenopathy (commonest), branchial cyst, cystic hygroma, dermoid cyst, thyroid lobe enlargement, pharyngeal pouch, cold abscess and sternocleidomastoid tumor (in infants). Clinical examination of the neck helps in differentiating the site and nature of the swelling to a large extent.

Diffuse enlargement of SCM in infancy is known to occur at around 3 weeks to 3 months of age. The cause is unknown although 'idiopathic intrauterine embryopathy'[2] and intrauterine positional disorder with development of 'sternocleidomastoid compartment syndrome'[3] has been postulated for its genesis. The basic change in histopathology is fibrous replacement of muscle bundles. A process of endomysial fibrosis involves deposition of collagen and fibroblasts around individual muscle fibers that undergo atrophy.[2,4] The natural history of untreated sternomastoid fibrosis is complete resolution in 50% to 70% of patients at 6 months of age. In less than 10% of cases SCM shortening persists beyond 1 year of age.[5]

Shortening of SCM leads to ipsillateral torticollis which on longterm can lead to hemifacial hypoplasia (due to lack of muscular traction, the mandible and maxilla undergo hypoplasia), plagiocephaly in infancy and compensatory scoliosis in an older child.

In our case, there was spontaneous enlargement of the left SCM in its entire length, which was supple, and without shortening or lengthening failure, so there was no torticollis or limitations in rotation of the neck. The lack of symptoms was so distinct that the decision of excision was taken only due to progressively increasing swelling of the entire SCM and the uncertain nature of the pathology, in addition to concern for cosmesis. Debulking was not considered an option due to fear of recurrence. Post excision histopathological examination revealed hyperplasia of the muscle spindles with chronic inflammatory infiltrate with no atypia or granulomas. There was no fibromatous change seen in the muscle, thus differentiating it from sternomastoid tumor or fibromatosis coli.

Some studies[6-10] have shown that the use of progesterone, anti-estrogens, nonsteroidal antinflammatory drugs, warfarin, vitamin K and ascorbate in various combinations bring some response in halting the

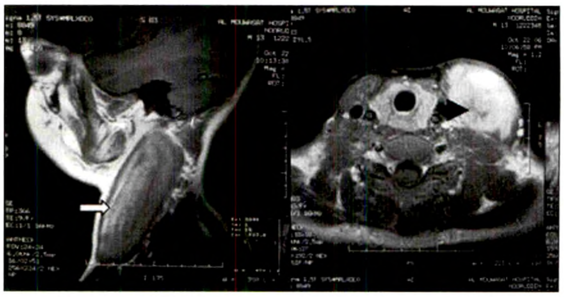

Figure 2. MRI of neck showing diffuse enlargement of left SCM (isointense on T1 (open arrow) and mildly hyperintense on T2 and enhancing after IV contrast (block arrow).

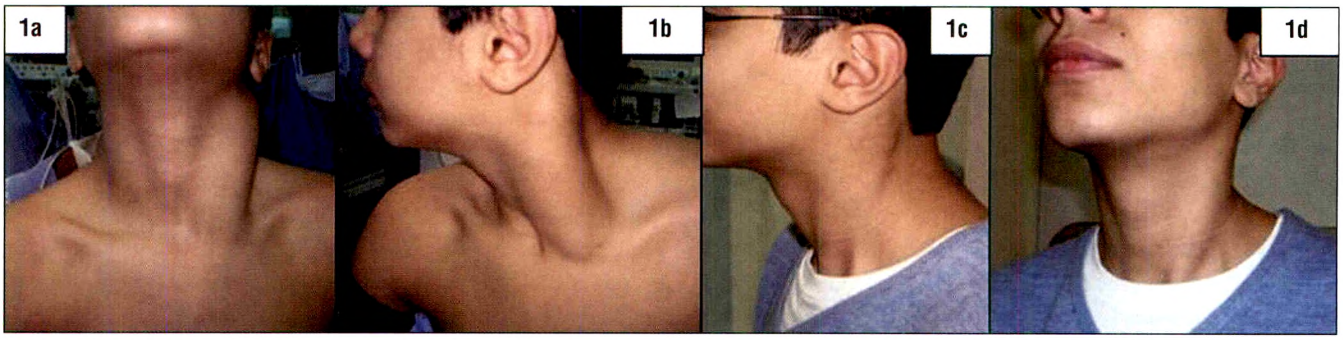

Figure 1. Diffuse enlargement of left sternocleidomastoid muscle without torticollis. Preoperative (1a and 1b); postoperative (1c and 1d) status.

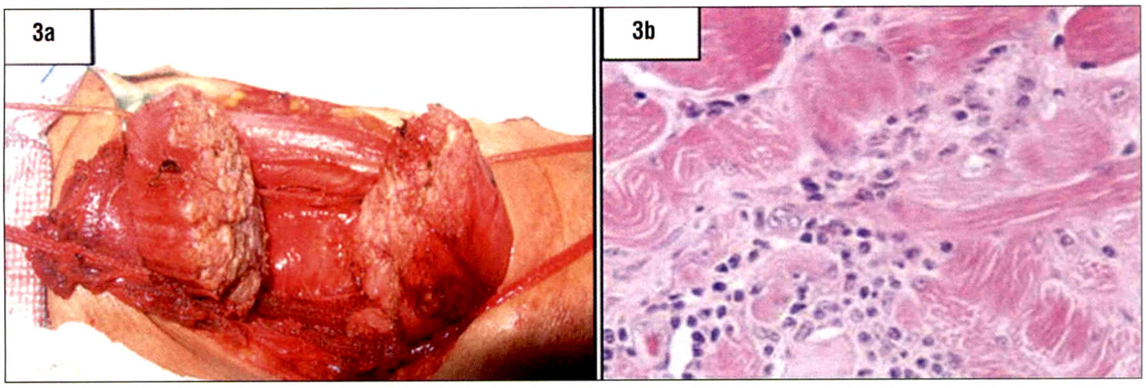

Figure 3. Gross (3a) and histopathology (3b) of excised left SCM showing hyperplasia and chronic inflammatory cell infiltration.

fibromatosis, mostly in desmoid tumors, but not so in infantile fibromatosis coli or sternocleidomastoid tumors. Therefore, the reasonable approach for treatment of even fibromatosis of the head and neck is complete surgical excision to avoid recurrences.[11] However, in our case there was no fibromatous change (rather there was hyperplasia of muscle) seen in the muscle, thus differentiating it from sternocleidomastoid pseudotumor or fibromatosis coli and precluding the option of anti-inflammatory drug therapy.

Idiopathic hyperplasia of SCM, as we have coined this entity in our case, is a nonfibromatous enlargement of the SCM, spontaneous in onset, histologically characterized by chronic inflammatory cell infiltrate limited to the SCM only and associated with no shortening or lengthening failure or torticollis. Muscle function is essentially preserved. Further study is needed to understand the natural course of this entity.

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case report

Hepatic vasculitis mimicking liver abscesses in a patient with systemic lupus erythematosus

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· Accepted for publication May 2009

Ann Saudi Med 2009; 29(6): 474-477

PMID: 19847087 DOI: 10.4103/0256-4947.57172

Clinical and radiological liver diseases are uncommon in patients with systemic lupus erythematosus (SLE). We report a 29-year-old female with SLE who presented with right upper quadrant abdominal pain, thrombocytopenia, elevated liver enzymes and multiple hypodense lesions in the liver on a computed tomography (CT) study that mimicked multiple liver abscesses. A liver biopsy showed mild chronic inflammation. Culture results were negative. With steroid therapy the patient improved clinically, the platelet count returned to the normal range and the multiple liver lesions disappeared radiologicaly. This patient represents a rare case of SLE that had hepatic vasculitis mimicking multiple liver abscesses.

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of unknown cause which can affect the skin, joints, kidneys, lungs, nervous system and other organs of the body. Immunologic abnormalities, especially the production of a number of antinuclear antibodies, are another prominent feature of the disease. The clinical course of SLE is variable and may be characterized by periods of remissions, chronicity or acute relapses. Women, especially in their 20s and 30s, are affected more frequently than men. Although biochemical evidence of liver disease is common in patients with SLE, clinical liver disease is uncommon.[1] We reported here a case of SLE that presented with right upper quadrant pain and multiple liver lesions secondary to hepatic vasculitis.

CASE

A 29-year-old woman known to have SLE for 6 years presented to the emergency department with a 5-day history of upper abdominal pain. She described the abdominal pain as dull and crampy, mild to moderate in intensity and localized to the epigastric and right upper quadrant regions. Two days before admission, the abdominal pain became constant and severe, and associated with nausea and vomiting but not associated with positional changes, eating, bowel movements or other factors. There had been no fever, chills, diarrhea, heartburn, hematemesis, melena or hematochezia. There was no history of herbal use, taking any new drugs or ingestion of unusual or undercooked foods and no recent travel or contact with ill persons. She was not known to have drug allergies and had no history of cigarette use, alcohol drinking or drug abuse.

She had been discharged from the hospital 2 weeks previously due the intrauterine death of her fetus at 30 weeks gestational age. She had been treated for SLE with low-dose prednisolone, with the addition of azathioprine and hydroxychloroquine and was maintained on pantaprazole as gastric prophylaxis. Her family history was notable for her mother who also had SLE.

On physical examination, the patient was afebrile. Her blood pressure was 158/90 mm Hg, pulse rate was 117 beats per minute, respiratory rate was 22 breaths per minute and oxygen saturation was 97% while breathing room air. The patient appeared to be in severe pain, with a pain score 8/10, and there were no jaundice, pallor, skin rash or mouth ulcers. The lungs and heart sounds were normal. Abdominal examination yielded right upper quadrant tenderness with no guarding or rebound tenderness, normal bowel sounds and no palpable organomegaly or masses. Results of the remainder of the complete multisystem examination were unremarkable.

Laboratory studies revealed the following: serum sodium 132 mmol/L, potassium 4 mmol/L, and creatinine 54 µmol/L. A complete blood cell count revealed a hemoglobin level of 103 g/L, mean corpuscular volume 90 fL, mean corpuscular hemoglobin 30 pg, a white blood cell count of 10.8×10^9/L, an absolute neutrophil count of 9×10^9/L, lymphocyte count of 1×10^9/L, and an eosionophil count of 0.2×10^9/L, and a platelet count of 39×10^9/L. The hemolysis markers were normal. Serum iron saturation was 30%. Prothrombin time was 9.9 sec, partial thromboplastin time 34.2 sec, international normalized ratio of 1.1 and the fibrinogen level was normal. Serum liver biochemistry results showed a total bilirubin of 23.6 µmol/L and a direct bilirubin of 13.1µmol/L, alkaline phosphatase of 161 U/L, aspartate aminotransferase of 354 U/L, alanine aminotransferase of 429 U/L, albumin of 37 G/L. Serum amylase was normal. Stool examination for ova, parasites, and occult blood were negative. Urine analysis was normal. The erythrocyte sedimentation rate was elevated 125 mm/h. The complement levels were normal. Serologic studies revealed a positive antinuclear antibody test of 123.7 units and anti-ds-DNA test 200 units. Anti-SM, anticardiolipin antibody, antimitochondrial antibody, and anti-smooth muscle antibody were all negative. Immunoglobulin G was elevated at 26.5 g/L, and immunoglobulin M was normal. Viral hepatitis B and C screening tests were negative. The thyroid function test, vitamin B12 and folate levels were all normal. A chest radiograph, electrocardiogram and serum cardiac enzymes were all within normal limits. A computed tomography scan of the abdomen showed a normal liver size with multiple irregular hypodense lesions, mainly in the right hepatic lobe, which did not show arterial or venous enhancement (Figure 1)

The patient was diagnosed initially with SLE flare up with liver involvement and autoimmune thrombocytopenia. She was started on high-dose methylprednisolone, 1 gram intravenously daily for 5 days, and intravenous immunoglobulin for 3 days. On the second day of management the pain dramaticaly disappeared and the liver enzymes started to improve as well as the platelet count. The patient initially was covered with broad spectrum intravenous antibiotics (pipracillin-tazobactam and metronidazole) due to the possibility of pyogenic or amoebic liver abscess, but since there was no evidence of infection, clinically or by laboratory investigation, and the her condition improved clinically and biochemically in the second day after receiving pulse steroids, the antibiotics were discontinued.

An ultrasound-guided biopsy from the liver lesions was non-conclusive, showing mild congestion and chronic mild inflammation with no granulomatous or atypical changes. Results of cultures from blood, urine and stool were negative. Amebiasis antibody was negative. She was discharged in good condition with no pain and normal liver enzymes and platelet count. Discharge medications included prednisolone tablet 40 mg daily and resumption of previous medications. A follow up CT-scan abdomen one month from discharge showed complete resolution of the previous lesions in the liver with normal liver parenchyma.

DISCUSSION

Although overt liver disease has been rarely described in patients with SLE, subclinical manifestations or biochemical abnormalities are not uncommon. In one retrospective study of 238 SLE patients, 60% were found to have liver function abnormalities, with 24% having presenting symptoms consistent with hepatitis. The diagnosis of liver disease in SLE usually occurred one or more years after the diagnosis of SLE.[1] The presence of elevated liver enzymes and clinical symptoms of hepatitis correlated with a lupus flare in 21%.[1] In another retrospective study of 81 cases, liver abnormality might have been related to SLE itself in 19 of 45 cases who had abnormal liver enzymes.[2] In a prospective study, hepatic enzyme elevation was observed in 23% of 260 lupus patients, of which the cause of liver enzyme abnormalities was not identifiable in 8%. However, this cause was related to the activity of lupus in 8% of the cases,[3] and the majority of biochemical abnormalities seen in these studies were usually secondary to other causes such as drug-induced liver dysfunction, alcohol, liver congestion from congestive heart failure, infection or metabolic disturbances. Hepatomegaly (39% to 42%) and jaundice (24%) were often seen at the onset of liver disease.[1,2] Various forms of hepatic pathology related to SLE have been described, and they include fatty liver,[2,4] portal inflammation,[2] chronic active hepatitis,[1,2] chronic persistent hepatitis,[1,4] cirrhosis,[1] cholestasis,[1,4] hepatic necrosis associated with antiphospholipid antibody syndrome,[5] granulomatous hepatitis,[1] non-specific reactive hepatitis,[4] nodular regenerative hyperplasia,[4] hepatic infarction[4] and arteritis.[4,6,7]

Although granulomatous hepatitis has been described in SLE, it is uncommon. It was found in 4 of 33 (12%) histological-proved liver diseases in SLE reported by Runyon et al.[1] Two of these patients also had hepatomegaly, and one had a lupus flare. Feurle et al reported a case of granulomatous hepatitis, which man-

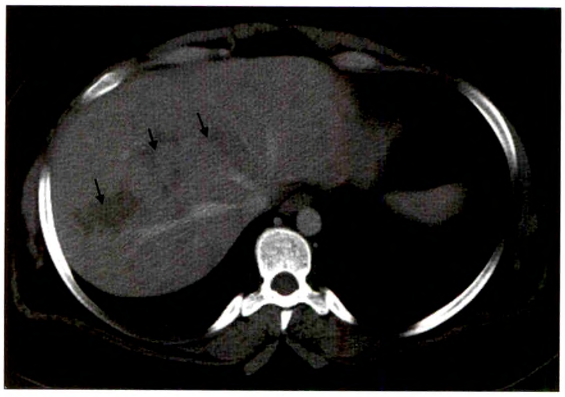

Figure 1. A computed tomography scan of the abdomen with intravenous contrast presents hypodensities with no appreciable enhancement distributed in an irregular patchy and linear form. Some of the distribution simulates the cluster sign of abscesses.

ifested biochemically as an elevation of alkaline phosphatase during a flare-up of SLE.[8] Among the older reports, Harvey et al found two cases of hepatic vasculitis and two of hepatic granulomas.[7] Kofman et al described granulomatous hepatitis in one of 11 liver pathological specimens.[9] In Aronson's series of 19 autopsy-proved cases of SLE, hepatic granuloma was observed in 5%. None of these cases had severe liver diseases.[10]

Conflicting data on the incidence of hepatic vasculitis in SLE have been reported. In a report of the 33 histologically proved liver diseases in SLE by Runyon et al, none had vasculitis.[1] In contrast, hepatic arteritis was found in 11 cases from 52 (21%) pathologically proved liver diseases in SLE from the Japanese autopsy registry.[4] Miyake et al reported a young Japanese man with acute SLE, elevated transaminase, and multiple hypodense spots in the liver in a CT study.[11] A biopsy specimen from a low-density spot lesion showed mild inflammatory cell infiltration and piecemeal necrosis. These hypodense lesions may be due to vasculitis, as corticosteroid therapy improved the patient's clinical status, normalized laboratory abnormalities and caused the liver lesions to disappear. Fehr et al reported a case of liver necrosis in an SLE patient with antiphospholipid syndrome, who also had HELLP (Hemolysis, Elevated Liver enzymes and Low Platelet count)-like syndrome. A CT scan of the liver also showed multiple hypodense lesions, and biopsy revealed periportal necrosis with fibrin deposit and accumulation of sinusoidal granulocytes. Anticoagulant and immunosuppressive therapy improved the patient's clinical status.[5] The hypodense lesion in this case might be related to hepatic infarction secondary to antiphospholipid syndrome. Spontaneous rupture of the liver, secondary to hepatic vasculitis, has been reported by Levitin et al.[6] However, the imaging study of the liver was not performed in this case.

Suparaporn et al reported a patient with SLE who had hepatic vasculitis with necrosis mimicking multiple liver abscesses as an initial presentation. Because of suspicion of pyogenic liver abscess the patient was not given steroid therapy and unfortunately she died. A biopsy specimen showed necrotizing granuloma with a large area of necrosis.[12] In our case the main concern was starting the patient on a high dose of corticosteroid because the pyogenic liver abscess was part of the differential diagnosis. However, because of the clinical scenario and the presence of autoimmune thrombocytopenia, high anti-DNA (Deoxyribonucleic acid), which indicates active SLE, and negative septic work up, the decision was to give the patient pulse steroid and IV immunoglobin. In addition to that the patient was initially covered with intravenous antibiotics for three days, which were discontinued because of the dramatic response to pulse steroids in a very short time. The lack of significant enhancement of the lesion is supportive of the absence of an infectious component and the linear fashion suggests possible periportal vascular insult. The negative test for anticardiolipin antibody and lupus anticoagulant made the possibility of hepatic infarction secondary to antiphospholipid syndrome unlikely.

The patient was discharged on high dose of oral steroid for one month. The repeated CT scan four weeks later showed complete resolution of the these multiple liver lesions. The presence of active SLE disease and the complete recovery (clinically and radiologicaly) with high-dose steroid supported the diagnosis of hepatic vasculitis as a cause of this patient's multiple liver lesions, which mimic multiple liver abscesses.

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case report

Lymphoepithelioma-like carcinoma of the urinary bladder: report of a rare case

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Ann Saudi Med 2009; 29(6): 478-481
PMID: 19847088 DOI: 10.4103/0256-4947.57173

Lymphoepithelioma-like carcinoma (LELC) is a rare malignant neoplasm in the urinary bladder, which can histologically mimic lymphoma, poorly differentiated invasive transitional cell carcinoma or poorly differentiated squamous cell carcinoma with a lymphoplasmacytic background. A urinary bladder tumor was identified in a 65-year-old man suffering from hematuria for several weeks. Transurethral biopsy revealed an undifferentiated tumor with prominent lymphocytes and plasma cell infiltration. Immunohistochemical evaluation showed positive staining for cytokeratin and epithelial membrane antigen. Subsequent radical cystectomy showed pure LELC. We present the case to highlight the significance of recognizing this unusual bladder tumor and discuss the important differential diagnosis, treatment options and prognosis.

Lymphoepithelioma is the term used for describing an undifferentiated carcinoma of the nasopharynx, histologically characterized by the presence of prominent lymphoid aggregates in the background. Carcinomas with similar histologic features arising outside the nasopharynx are called lymphoepithelioma-like carcinoma (LELC), which are reported in various organs such as the thymus, salivary gland, and cervix. Involvement of the urinary bladder, first reported by Zuckerberg et al in 1991,[1] is uncommon, with a reported incidence between 0.4% and 1.3% of all bladder carcinomas.[2] The tumor can occur either in pure form or in association With conventional urothelial carcinoma.[3] The pure form is considered to have a better prognosis and exhibits a good response to chemotherapy.[2-5] It is important to differentiate LELC from non-Hodgkin lymphoma, poorly differentiated invasive transitional cell carcinoma and poorly differentiated squamous cell carcinoma with lymphoplasmacytic infiltrate in the background. We report a case of pure LELC of the urinary bladder in a 65-year-old man and discuss the important differential diagnosis, various treatment options and the prognosis of this unusual tumor. To our knowledge, this is the first reported case of LELC of the urinary bladder from the Middle East.

CASE

A 65-year-old man presented with a history of recurrent painless hematuria for several weeks. There was no history of other urological complaints. Cystoscopy showed a sessile ulcerated lesion measuring about 3 cm in diameter, in the right posterolateral wall of the bladder. A CT scan revealed a soft tissue tumor mass in the right posterolateral aspect of the urinary bladder wall involving the right ureteric orifice, with a consequent right-sided hydroureter (Figure 1). There was no evidence of perivesical spread of the tumor or metastatic disease elsewhere. Transurethral resection of the tumor was attempted. The biopsy was reported as LELC with infiltration into the muscularis propria. Subsequently, a radical cystectomy obtained a specimen that measured 8.5×7×4 cm. A cut section revealed an ulcerated tumor mass measuring 3×3×1.5 cm at the right posterolateral wall of the bladder. On microscopy, the tumor was composed of diffuse sheets and cords of undifferentiated cells having large pleomorphic nuclei with coarse chromatin (Figures 2 and 3). Many of the nuclei had prominent nucleoli. The cytoplasm was moderate with poorly defined borders. The background showed dense lymphoplasmacytic infiltration with occasional eosinophils. The tumor showed transmural infiltration, but not invading the perivesical adipose tissue. There was no evidence of an in situ component in any of the examined sections. The entire tumor demonstrated similar morphology, without any associated component of conventional urothelial type carcinoma, or any other subtypes, such as squamous cell carcinoma or adenocarcinoma. The tumor cells were positive for pan cytokeratin (CK) (Figure 4), CK7, CK 8 and Epithelial Membrane Antigen, but negative for chromogranin, vimentin and desmin. A diagnosis of pure LELC with evidence of muscular invasion was entertained. The patient had an uneventful post operative period. He is currently on follow-up and is free of symptoms, 12 months after the surgery.

DISCUSSION

LELC is a rare variant of infiltrating urothelial carcinoma, first described by Zuckerberg et al in 1991.[1] Since then there have been only a few relatively small studies on LELC of urinary bladder. [2-8] The largest study was reported by Tamas et al[8] who described 17 pure 13 mixed LELC. Prior to that Lopez-Beltran et al[5] reported 3 pure, 6 predominant and 4 focal LELCs of the urinary bladder. Amin et al[3] reported 3 pure, 5 predominant and 3 focal LELCs and Holmang et al[6] described 3 pure, 5 predominant and 3 focal cases of LELC. To our knowledge, LELC of the urinary bladder has not been reported from the Middle East to date.

The exact pathogenesis of this tumor is not well established. Epstein-Barr virus (EBV) is frequently associated with lymphoepithelioma of the nasopharynx and LELC arising in the lung, stomach, thymus and salivary gland.[1,2,8,9] However, such an association has

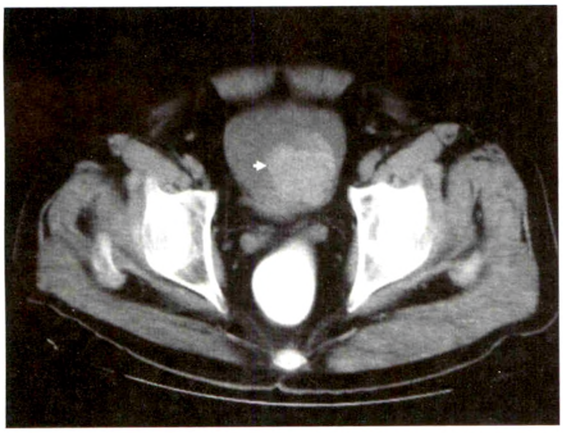

Figure 1. Contrast-enhanced CT scan showing moderately enhancing lobular intravesical mass lesion (arrow) arising from the base of the urinary bladder, involving the right vesicoureteric junction.

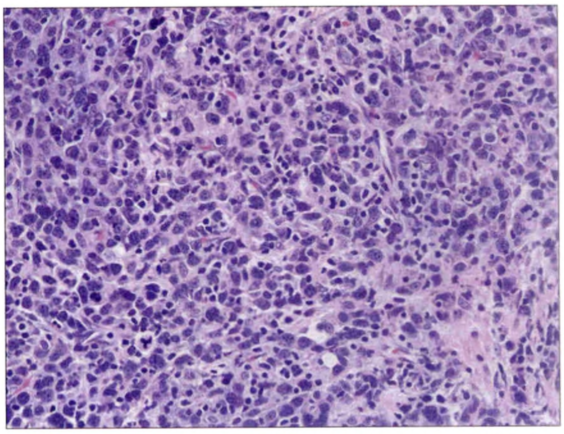

Figure 3. Undifferentiated tumor cells with vesicular nuclei and indistinct cell margin along with few interspersed lymphocytes and plasma cells (hematoxylin-eosin stain ×400).

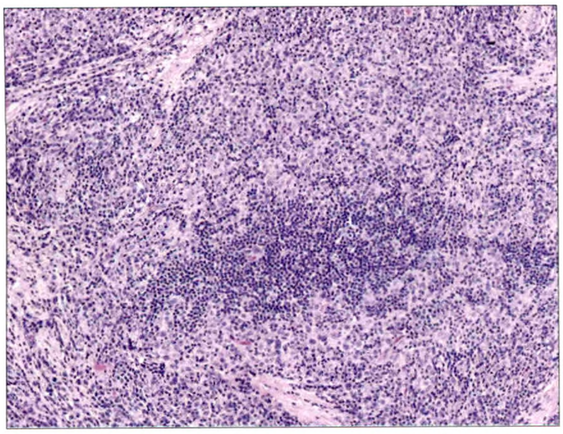

Figure 2. Photomicrograph demonstrating diffuse sheets of pleomorphic tumor cells admixed with prominent inflammatory infiltrate (hematoxylin-eosin stain ×200).

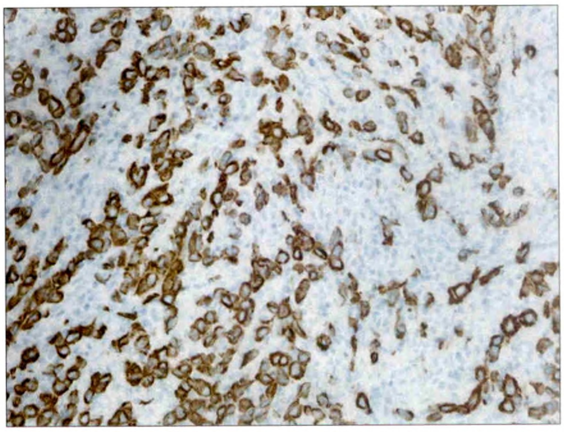

Figure 4. Immunohistochemical stain for pancytokeratin, highlighting tumor cells with unstained lymphocytes in the background (immunoperoxidase stain ×400).

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not been documented for LELC of the urinary bladder. Hybridization with EBV-encoded RNA (EBER) has been reported to be negative.[5,8,9] It has been suggested that abnormalities of p53 regulation might be crucial in the pathogenesis of LELC of the urinary bladder.[10] Though the exact origin of these carcinomas is not well known, the expression of common urothelial markers suggest that they are probably modified urothelial cells that have derived from stem cells.[5,6]

The tumor usually presents in late adulthood. Most patients present with painless hematuria and are stage T2-T3 at diagnosis.[5,6,8] Histological features of LELC closely resemble lymphoepithelioma of the nasopharynx, with the tumor growing in nests, sheets or cords of large undifferentiated malignant epithelial cells within a dense inflammatory background, comprising mature lymphocytes, plasma cells, and rarely neutrophils and eosinophils. The background lymphocytes are usually an admixture of B and T lymphocytes.[11] Amin et al[3] categorized the LELC of bladder into three subgroups as pure, predominant (more than 50% lymphoepithelial component) and focal (less than 50% lymphoepithelial component). Invasive urothelial carcinoma usually accompanies predominant or focal LELC.[3,5,8] Though uncommon, the tumor may have accompanying adenocarcinoma and squamous cell carcinoma as well.[5,8] The overlying or adjacent urothelium may show urothelial dysplasia or carcinoma in situ.[2,8] The present case was a pure LELC. A correct diagnosis on a urine cytology specimen can be particularly challenging, considering the rarity of the tumor. Cai and Parwani[12] reported cytologic findings in two cases of LELC of the bladder, which were confirmed by histopathological examination of the resected tumor. Useful cytomorphologic features include the presence of large tumor cells with a high nuclear-to-cytoplasmic ratio, vesicular chromatin and prominent nucleoli, presenting as single cells or intermixed with inflammatory cells.[12]

Pure LELC must be distinguished from reactive inflammatory lesions or lymphoma. Primary lymphoma of the bladder is extremely rare, and has an entirely different therapeutic approach.[3] Immunohistochemistry for cytokeratin and lymphoid markers can help in resolving this differential diagnosis. Owing to the presence of a prominent inflammatory background, the neoplastic cells may be assumed to be reactive histiocytes and the lesion may be misdiagnosed as chronic cystitis.[1,3] Hence, a dense lymphoid infiltrate in a urinary bladder biopsy should alert the pathologist to closely look for neoplastic cells. Immunohistochemistry for epithelial markers can be helpful in highlighting the neoplastic cells in such instances. Other important differential diagnoses include poorly differentiated invasive transitional cell carcinoma or poorly differentiated squamous cell carcinoma with associated dense lymphoplasmacytic infiltrate.[3,13] Sometimes, it might be problematic to differentiate LELC from small cell carcinoma of the urinary bladder or prostate in small, improperly fixed biopsy specimens with crush artifacts.[1,3]

Most of the previous studies have suggested that LELC has a relatively favorable prognosis when in pure or predominant forms with reported rates of metastasis ranging from only 12% to 15%.[2,3,5] Amin et al[3] reported on three patients having pure LELC and five patients having predominant LELC, all of whom showed no evidence of disease (2-72 months). In contrast, the two patients with focal LELC succumbed to metastatic disease 6 and 84 months after diagnosis. Similarly all the three patients in the study by Holmang et al[6] with focal LELC died of the disease (9-68 months), compared to none of the six patients with pure or predominant LELC (13 months to 18 years). In the study by Lopez-Beltran et al,[5] all three patients with pure and 4/6 patients with predominant LELC were alive, while all four patients having focal LELC died of disease. However, Tamas et al[8] did not find any difference in prognosis between pure and mixed LELC. Their study demonstrated that LELC treated by cystectomy has a similar prognosis to ordinary urothelial carcinoma and does not differ between pure and mixed cases. In cases with cystectomy, the overall 5-year actuarial recurrence-free risk was 59% (62% and 57%, for pure and mixed LELC, respectively). The rationale behind this apparent better prognosis, however, has not been well investigated. It is known that tumors with lymphoid infiltration have a comparatively better prognosis than those without it. Intense immune response generated by these lymphoid cells against the tumor may play an important role in this regard.[3]

The paucity of published literature suggests that there is limited experience in therapeutic approaches to LELC of the bladder. The pure/predominant form may respond to chemotherapy.[3-5,8] In the study by Amin et al,[3] four of the pure/predominant LELC were treated with transurethral resection and chemotherapy and all showed no evidence of disease. Dinney et al[4] has shown a complete response to chemotherapy and transurethral resection of the bladder tumor in 3 cases of muscle invasive LELC. In another study by Lopez-Beltran et al[5] 2 of their 13 patients received chemotherapy and both showed no evidence of disease at 21 and 47 months. In a recent study by Tamas et al,[8] of the three pure cases treated by chemotherapy, two were free of disease at 4 and 65 months and the third had recurrent disease at 17 months. Our case underwent radical cystectomy without chemotherapy and was free of disease 12 months after surgery.

In conclusion, LELC of the bladder is rare and should be ruled out in bladder biopsies that show dense lymphoid infiltrate. The differential diagnosis is usually lymphoma, poorly differentiated invasive transitional cell carcinoma and poorly differentiated squamous cell carcinoma with lymphoplasmacytic background. Existing data suggest the pure form responds well to chemotherapy and has a better prognosis.

Acknowledgments

We are thankful to Dr. Sontenam VSMR of the department of Radiology, Al Jahra Hospital, Kuwait for providing the radiological details.

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case report

Poland-Mobius syndrome in an infant girl

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Ann Saudi Med 2009;29(6): 482-484

PMID: 19847089 DOI: 10.4103/0256-4947.57174

Mobius syndrome is a rare condition of unclear origin, characterized by a unilateral or bilateral congenital facial weakness with impairment of ocular abduction, which is frequently associated with limb anomalies. Poland described a condition in which there was unilateral absence of pectoralis major muscle and ipsilateral syndactyly. The combination of Poland-Mobius syndrome is rare, with an estimated prevalence 1:500 000. We describe a case of Poland-Mobius syndrome in association with congenital bilateral vocal fold immobility. To our knowldge, this is the first report of such an association between Poland-Mobius syndrome and congenital bilateral vocal fold immobility.

Poland-Mobius syndrome is a rare congenital disorder that includes combination features of Poland and Mobius syndromes. Poland syndrome consists of absence of pectoralis major muscle, syndactyly, barchydactyly and hypoplasia of the hands.[1] Mobius syndrome includes a variable degree of facial paralysis with an inability to abduct the eyes beyond midpoint.[1] Unilateral or bilateral vocal fold paralysis is a significant cause of stridor in infant and children. Neonatal bilateral vocal fold paralysis may be caused by birth trauma, asphyxia, or central nervous system (CNS) anomalies.[2] Other recognizable syndromes such as Down syndrome, 22q deletion syndrome, and Robinow syndrome can present with bilateral vocal fold paralysis.[3] In most cases of Mobius syndrome, unilateral vocal fold immobility is a frequent feature. We report an infant with macrocephaly, hypertelorism, low set ears, a restricted mouth opening, an expressionless face, upper limb anomalies and bilateral talipas equino varus. This may be the first reported case of Poland- Mobius syndrome associated with bilateral vocal fold immobility.

CASE

A 20-day-old Saudi infant girl referred for evaluation and management of respiratory distress to the Pediatric Otolaryngology service at King Abdulaziz Medical City. The patient was the first of identical (monozygous) female twins born at 34 weeks of gestation by caesarean delivery due to breech presentation. The Apgar score was 2 and 8 at 1 and 5 minutes, respectively. The weight of the girl was 1.85 kg, height 42.5 cm and her head circumference was 34 cm. The mother was G2P0 and her pregnancy resulted from *in vitro* fertilization (IVF). A positive history of consanguinity (first degree relatives) was reported. There were no dysmorphic features in the parents or siblings. The second twin had been discharged on the first day in good health status with no congenital abnormalities. At birth, the baby had cyanosis and respiratory distress. She was immediately intubated with difficulty and transferred to the neonatal intensive care unit (NICU). Examination showed a dysmorphic baby with macrocephaly (box-like skull) and a prominent parietal region with a high forehead. The baby also had hypertelorism, low set ears, a restricted mouth opening and an expressionless face (Figure 1). Her right upper limb appeared to be hypoplastic with 2nd, 3rd and 4th partial syndactyly and barchydactyly. Her right pectoralis major muscle was hypoplastic. The left hand had features of camptodactyly. Her lower limbs revealed bilateral talipes equinovarus. A possible diagnosis of Poland-Mobius syndrome was suggested. She was extubated after 3 days and transferred to the intermediate care unit of neonates (ICN). One week later, she developed severe respiratory distress and desaturation to 80%. Flexible nasoendoscopy showed moderate pharyngeomalacia and bilateral vocal fold immobility (Figure 2). Feeding was through the orogastric tube. Magnetic resonance imaging (MRI) of the brain showed normal brain tissue. Swallowing could not be evaluated due to fixed jaws.

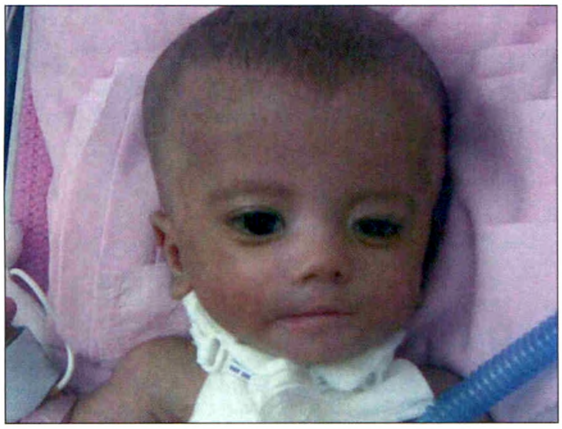

Figure 1. A photo of the infant showing some of the dysmorphic features (hypertelorism, low set ears, a restricted mouth opening and an expressionless face).

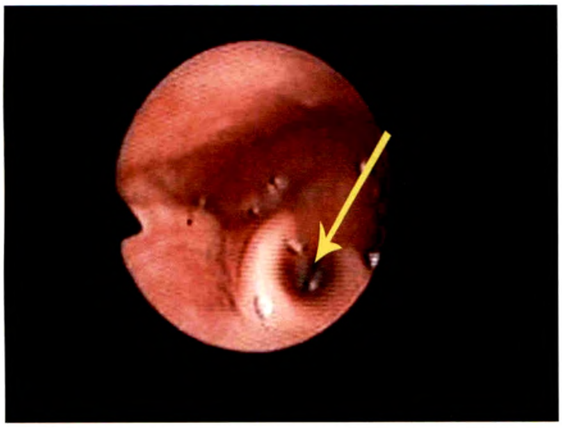

Figure 2. A still image of flexible nasoendoscopy showing the immobile vocal folds (arrow).

At the age of one month, a tracheotomy was needed because of recurrent attacks of respiratory distress and the anticipated possibility of difficult intubation. At the age of 2 months, the child underwent fundoplecation and gastrostomy tube because of dysphagia and gastro esophageal reflux disease (GERD). Chromosomal analysis of both twins showed a normal 46XX karyotype.

DISCUSSION

Mobius syndrome was first reported in 1880 by Von Greave and in 1888 by Paul Julius Mobius.[4] The syndrome consists of congenital complete or partial facial nerve paralysis with or without paralysis of other cranial nerves. The most common cranial nerve involved is the 6th cranial nerve (abducent). The oculomotor and trochlear can also be involved. It is also known as congenital facial diplegia, nuclear agenesis, congenital nuclear hypoplasia, congenital occulofacial paralysis and congenital abducens–facial paralysis.[1] According to the pathologic changes, Mobius syndrome is classified into four groups.[5] Group I is characterized by simple hypoplasia or atrophy of cranial nerve nuclei, presumably as a result of embryonic maldevelopment. Group II results from primary lesions in the peripheral portion of the cranial nerves. Group III is due to focal necrosis in the brain stem nuclei. Group IV consists of patients without lesions in the central nervous system or cranial nerves but showed features of primary myopathy.

The Mobius syndrome represents a distinctive malformation syndrome, but its etiology remains undetermined. Numerous theories exist concerning the primary underlying pathogenesis. Intrauterine vascular etiology involves disruption of the flow in the basilar artery or premature regression of the primitive trigeminal artries.[6] Toxic or a degenerative material which involves the nuclei of the affected nerves was suggested as alternative theory. Congenital inherited hypoplasia or agenesis of the CN nuclei, and infectious factors have been also proposed as important factors.

Poland syndrome was described in 1841 by Alfred Poland as unilateral absence of pectoralis major muscle and ipsilateral dermal syndactyly of the hand.[7] Other anomalies associated with this syndrome include hypoplasia of the forearm, hypoplasia of the breast, agenesis of the nipple, rib cage deformities, bilateral epicanthus and talipes equinovarus.[1] Boys are affected more than girls. The reported frequency is 1:20 000.[1] Ten percent of all cases of hand syndactyly may have the Poland sequence. The syndactyly is usually in the right hand as in our patient. Poland syndrome is not an inheritable condition nor one that arises from events during pregnancy, which was established in a detailed study of twins affected with Poland syndrome using DNA evidence to establish that they were identical.[8] Furthermore, since the both of the embryos, fetuses and newborns have been exposed to identical physical and chemical conditions, there were no environmental teratogenic sources implicated. This non-genetic and non-teratogenic etiology suggests that Poland syndrome is entirely sporadic.

The combinations of Poland and Mobius anomalies are rarely described in the literatures with an estimated prevalence of 1:500 000.[1,9-11] Some authors believe this association is an independent syndrome. Others think that Poland, Mobius and Poland-Mobius syndromes are variations of the same condition.[9]

Unilateral or bilateral vocal fold paralysis is a significant cause of stridor in infants and children.[2] Bilateral vocal fold paralysis is the second most common cause of stridor in the neonate. Flexible laryngoscopy is the main method for the diagnosis of vocal fold immobility. Neonates and infants with suspected vocal fold paralysis must be carefully evaluated for underlying diseases. Neonatal bilateral vocal fold paralysis may be caused by birth trauma, asphyxia or central nervous system anomalies.[2] It has been also described in some recognizable syndromes, including Down syndrome, 22q deletion syndrome, Robinow's syndrome and cerebro-oculo-facio-skeletal syndrome.[3] Up to our knowledge, no previous cases of Poland-Mobius syndrome with congenital bilateral vocal fold paralysis have been reported in the English literature.

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Uncommon osseous involvement in multisystemic sarcoidosis

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Ann Saudi Med 2009; 29(6): 485-486

PMID: 19847090 DOI: 10.4103/0256-4947.57175

A 50-year-old man with a past medical history of nephrolithiasis presented with right upper quadrant and flank pain. The physical examination was unremarkable. Routine lab investigations were normal. Angiotensin-converting enzyme levels were elevated, but hypercalcemia was not detected. A chest radiograph showed multiple bilateral nodules associated with hilar fullness and widening.

A CT scan of the chest and abdomen showed mediastinal and hilar lymphadenopathy, pulmonary nodules, and multiple ill-defined low-density lesions in the liver and spleen. A whole body fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) showed multiple FDG-avid foci throughout the vertebrae, left maxilla, right infraorbital region, left sphenoid, the scapulae, left clavicle, sternum, ribs, bilateral iliac crest, and proximal femora in addition to FDG-avidity in the pulmonary nodules and hilar area (Figures 1 and 2). Biopsy of the right iliac crest and a percutaneous liver biopsy revealed non-caseating granulomatous inflammation with asteroid bodies. The biopsy was negative for acid-fast bacilli, fungi, and malignancy (Figure 3).

Sarcoidosis is a multi-systemic disease of unknown etiology that predominantly affects the lungs and intra-

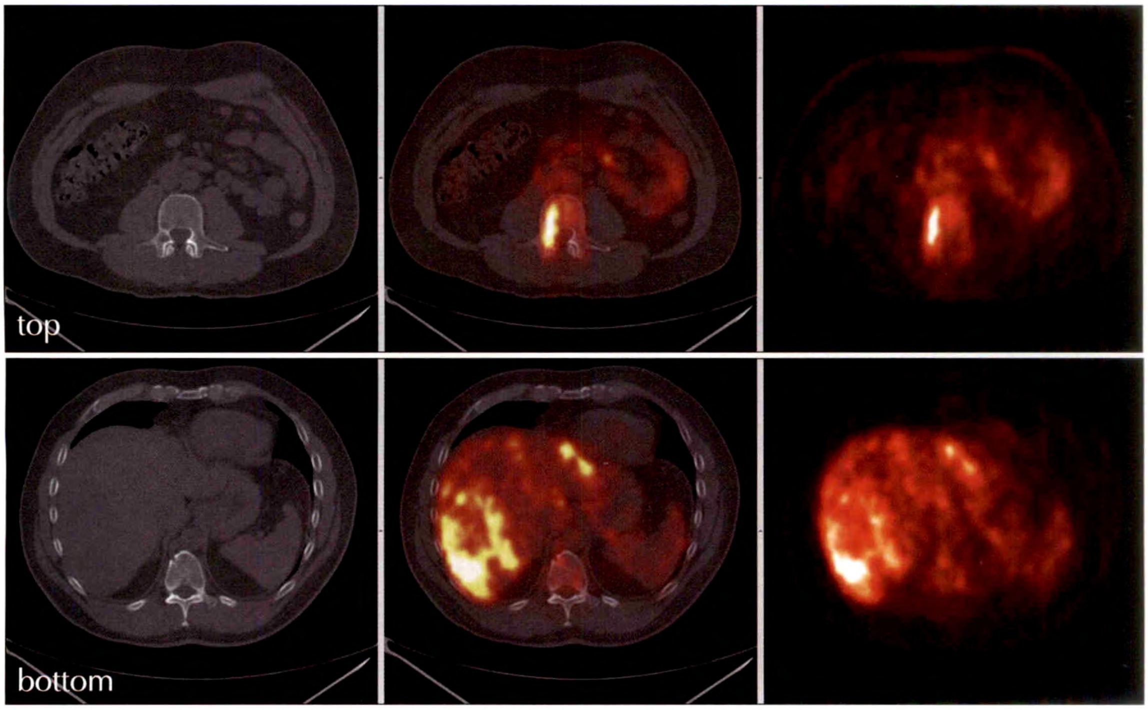

Figure 1. Lumbar vertebral (top) and hepatic involvement (bottom).

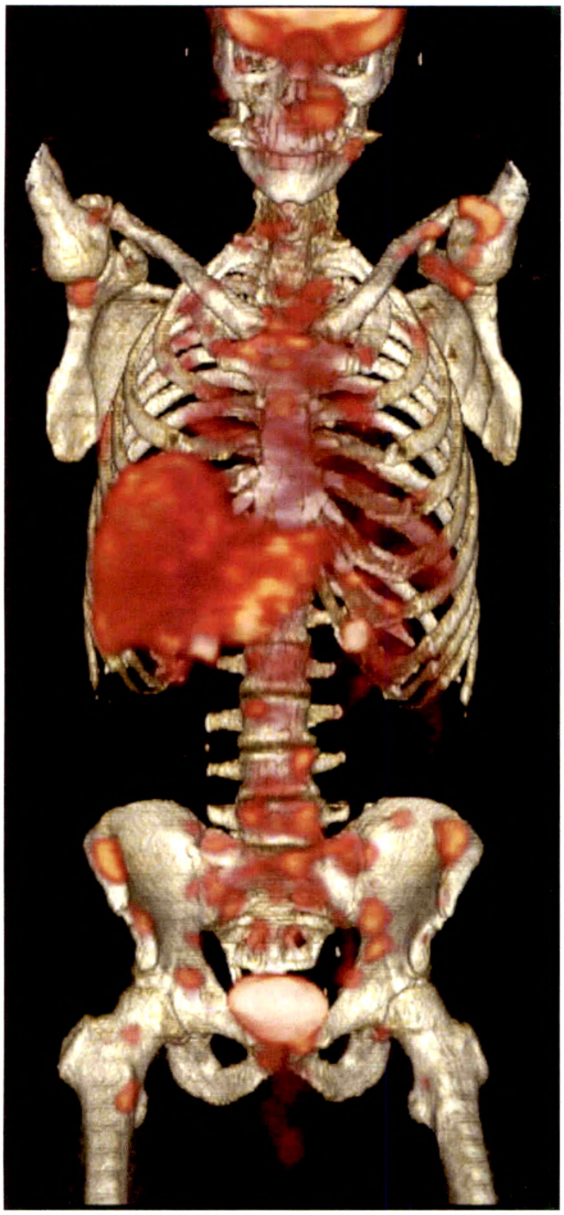

Figure 2. Maximum intensity projection image showing multiple foci abnormal hypermetabolic activity throughout the axial and appendicular skeleton.

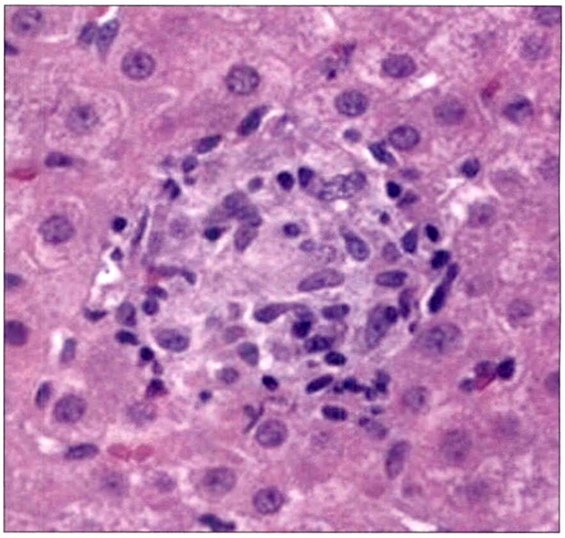

Figure 3. Hepatic biopsy showing non-caseous granuloma.

thoracic lymph nodes. Non-caseating granulomas are the pathological hallmark of sarcoidosis and disorders in T-cell function play a role in the pathogenesis of this disease.[1]

Osseous sarcoidosis has been reported in 1% to 14% of patients with sarcoidosis and usually involves the small bones of the hands and feet.[2] Involvement of vertebrae and long bones is extremely uncommon.With nonspecific accumulation of FDG into inflammatory cells, the disease can be visualized. The degree of FDG uptake has been related to activity of disease.[3]

The percentage of patients with osseous sarcoidosis may be underestimated. The FDG PET/CT scan may be a sensitive tool for evaluating the extent of bone involvement. Corticosteroids remain the major therapeutic option for symptomatic musculoskeletal sarcoidosis, but randomized, controlled trials are lacking.[4]

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Growth parameters and calcium homeostasis in cystic fibrosis patients with CFTR I1234V mutation

PMID: 19847091
DOI: 10.4103/0256-4947.57176

To the Editor: Cystic fibrosis (CF) is the most common life-threatening recessive genetic trait among whites.[1] Despite a recent emphasis on adequate nutrition, impaired growth occurs frequently in children with CF and the etiology appears to be multi-factorial.[1] Pancreatic insufficiency (PI) can be a major factor,[2] but other factors including insulin resistance, bone disease, hepatobiliary dysfunction and vitamin D deficiency may be significant risk factors for defective bone growth.[3] The cystic fibrosis transmembrane conductance regulator (CFTR) I1234V mutation, with normal exocrine pancreatic function, is a common mutation among Arabs in the Arabian Gulf region.[4]

Growth and nutritional parameters and FEV_1 were measured in 40 CF patients with CFTR I1234V mutation, (22 males and 18 females) from 22 families arising from a single large Arab kindred tribe attending the CF clinic at Hamad Medical Corporation, Qatar. The majority of patients were not taking regular nutritional supplements or vitamins. A single venous blood sample was obtained from each patient for measurement of circulating concentrations of 25-hydroxy vitamin D (25OHD) using DiaSorin 25-OHD radioimmunoassay kits (DiaSorin, Inc., Stillwater, Minnesota, USA), calcium, phosphorus, alkaline phosphatase (ALP), parathyroid hormone (PTH) intact molecule assayed by the electrochemiluminescence immunoassay [ECLIA] method (Elecsys 2010, Roche, Germany), and albumin. FEV_1 was measured with a flow-sensing spirometer (Sensor Medicus Model V6200, Germany). The mean height standard deviation score (HtSDS) was −0.46±1.0 and mean (SD) body mass index (BMI) was 20.8 (5.8) at a mean (SD) age of 11.9 (6.18) years. No patient showed clinical signs of rickets or osteomalacia. All patients had normal stool elastase activity, normal serum calcium with the median of 2.47 mmol/L (range, 2.21-2.66 mmol/L), phosphorus 1.54 mmol/L (range, 0.9-2.19 mmol/L), and ALP 171 U/L (range, 44-382 U/L). The mean (SD) circulating 25OHD concentration was 21.25 (3.42) ng/mL with 60% of patients <20 ng/mL (reference values, ≤10 ng/mL severe deficiency, 10-20 ng/mL mild to moderate deficiency and >20-80 ng/mL optimal). A mild elevation of serum ALP was found in 5/40 and increased serum PTH (67-77 pg/mL; normal range 9-65 pg/mL) was detected in 6 patients. The mean (SD) concentration of 25OHD was lower in adolescents >12 years of age vs those ≤12 years (15.8±7.63 vs 24.067±13.21 ng/mL). Moreover, circulating concentrations of phosphate and ALP were lower in the adolescents (>12 years) versus children ≤12 years (1.31±0.22 vs 1.84 ±0.23 mmol/L and 132.70±62.56 vs 229.40±62.57 U/L), respectively. Serum PTH concentration was lower in young children (<5 years) vs older children (≥5 years) and adolescents with CF (36.40±22.72, 48.43±14.03 and 47.75±16.85 pg/mL, respectively). HtSDS and FEV_1 showed no difference between patients with or without vitamin D deficiency (*P*=.76 and 0.2, respectively). HtSDS was correlated with FEV_1 (r=0.30; *P*<.05) and ALP (r=0.57; *P*<.01). Neither FEV_1 nor BMI correlated with 25OHD concentrations.

The high prevalence of vitamin D deficiency in our CF patients, despite normal pancreatic exocrine function, might be related to the hot weather and the usual clothing that covers most of the body, decreasing effective sun exposure. An intermittent increase of PTH secretion during vitamin D deficiency (n=6) is known to be an adaptive mechanism to increase alpha-hydroxylation of vitamin D and to maintain both normal serum calcium concentration and bone growth. However, when PTH levels become excessive or persistently high for long periods, osteopenia/osteoporosis may occur.

Our adolescent patients with CF had significantly lower serum levels of calcium, phosphate and ALP and a higher PTH level compared to young patients. This suggests better adaptability of young children to vitamin D deficiency compared with adolescents, and this may also mean that time is needed to develop clearer signs of vitamin D deficiency. The positive correlation between FEV_1 and HtSDS suggests the importance of good lung function for normal linear growth in these children. In summary, CF patients with the CFTR I1234V mutation showed normal linear growth and BMI and a high prevalence of vitamin D deficiency, suggesting that pancreatic exocrine function plays a major role in maintaining normal growth in patients with CF. Measurements of circulating vitamin D and PTH concentrations appear to be helpful for the early detection of abnormal calcium homeostasis in these patients.

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STROBE **(STrengthening the Reporting of OBservational studies in Epidemiology)** is an international, collaborative initiative of epidemiologists, methodologists, statisticians, researchers and editors involved in the conduct and dissemination of observational studies.

CONSORT (Consolidated Standards of Reporting Trials), is part of a broader push to produce reporting guidelines (RGs) for many different types of research. The main product of CONSORT is the CONSORT Statement, which is an evidence-based, minimum set of recommendations for reporting RCTs. It offers a standard way for authors to prepare reports of trial findings, facilitating their complete and transparent reporting, and aiding their critical appraisal and interpretation. The CONSORT Statement comprises a 22-item checklist and a flow diagram, along with some brief descriptive text.

ASSERT

The ASSERT **(A Standard for the Scientific and Ethical Review of Trials)** initiative is a proposed standard for the review and monitoring of randomized clinical trials by research ethics committees. Among other items, its checklist incorporates certain elements of CONSORT, to ensure fulfillment of the requirements for scientific validity in the ethical conduct of clinical research.

MOOSE

The MOOSE **(Meta-analysis of Observational Studies in Epidemiology)** paper reports the outcome of a 1997 workshop to examine the reporting of meta-analyses of observational studies. It makes recommendations to aid authors, editors, reviewers and readers of observational research.

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The QUOROM **(Quality Of Reporting Of Meta-analyses)** conference resulted in the creation of the QUOROM Statement, which consists of a checklist and flow diagram.

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The 22nd Saudi Urological Conference

15-18 March 2010
King Fahad Cultural Center
Riyadh, Saudi Arabia

Contact:
T: +966-1-442-7754
urology@kfshrc.edu.sa

3rd International Saudi Orthopaedic Association Conference

18-22 January 2010

Department of Orthopaedic Surgery, King Faisal University will be organizing the 3rd International Saudi Orthopaedic Association Conference in Alkhobar from 18th to 22nd of January 2010.

Prof Ibrahim Al-Habdan
Chairman Organizing Committee,
3rd Saudi Orthopaedic Association Meeting
AlKhobar, Saudi Arabia
18-22 January 2010

1st Saudi Surgical Residents Annual Research Day

The Department of Surgery in King Faisal Specialist Hospital & Research Centre, in collaboration with the Saudi Commission for Health Specialties, will be launching the 1st Saudi Surgical Residents Annual research Day on 04 February 2010 (20 Safar 1431) at the Four Seasons Hotel, Al-Mamlakah Tower, Riyadh. All surgical residents are invited to submit their novel research abstracts until 14 December 2009 (27 Dhu Al Hijjah 1431)

For more information, plese contact:
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Saudi Colorectal Surgery Forum

27-31 March 2010
Four Seasons Hotel, Al Mamlakah
Riyadh, Saudi Arabia

Dr. Alaa Abduljabbar,
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السمات السريرية ونتائج التصوير المقطعي لدى المرضى العرب الذين تم تشخيص حالتهم بغرناوية رئوية

مقدمة: وصف السمات السريرية ونتائج التصوير المقطعي CT لدى المرضى العرب الذين يعانون من غرناوية رئوية.

المرضى والطرق: أجريت دراسة مراجعة عن ديموغرافيا المرضى، والأعراض والأمراض المرضية، مرحلة الغرناوية، العلاج والوظائف الرئوية، ونتائج التصوير المقطعي CT.

النتائج: من بين ١٠٤ من المرضى، كانت الأغلبية (٧٧٪) في الـ ٤٠ من العمر أو أكبر سناً عند إجراء التشخيص، وفاقت أعداد المرضى الإناث بشكل ملحوظ المرضى الذكور (٦٦,٣٪ مقابل ٣٣,٧٪ ، بي= ٠٠٣). وتمثلت الشكاوى الشائعة في انقطاع النفس ٧٦٪، السعال ٧٢,١٪، فقدان الوزن ٣٢,٧٪. وقد تبين أثناء الكشف أن أغلب المرضى يعانون من معالم ضعف وظائف الرئة. من جهة أخرى، كان هناك ضعف في السعة الحيوية القسرية FVC (أكثر من ٥٠ ٪) لدى ١٧٪ فقط من المرضى. وتمثلت النتائج الأكثر تواراداً للتصوير المقطعي CT في تضخّم العقد اللمفية المنصفية لدى ٤٩ من المرضى (٧٣,١٪). لوحظ إصابة ٣١ من المرضى (٤٦,٣٪) بشذوذات متنية تدل على تليف رئوي، وشكّل توسع القصبات الهوائية بانكماش المتن، النمط التليفي الأكثر شيوعاً (٣٥,٨٪) في كشف التصوير المقطعي CT.

الاستنتاج: يبدو أن المظاهر السريرية للغرناوية في هذه العينة من المرضى العرب مشابهة لتقارير مرضى من شعوب أخرى. ويوجد هناك حاجة لإجراء المزيد من الدراسات للكشف عن مدى تأثير الأصل والعرق على شدة المرض في الشرق الأوسط.

الخزعة الكلوية للمصابين بداء السكري من النوع ٢: مؤشرات الآفات وطبيعتها

مقدمة: يختلف انتشار المرض الكلوي غير الناجم عن داء السكري كثيراً بين المصابين بداء السكري من النوع ٢ اعتماداً على المعيار الذي تم تحديده والأشخاص الذين أجريت عليهم الدراسة. كان الهدف من هذه الدراسة هو تقييم الخزعات التي تم أخذها من المصابين بداء السكري من النوع ٢ والمشتبه بإصابتهم بالمرض الكلوي غير السكري، ولإعادة ربط نتائج الفحص الباثولوجي بنتائج الفحص السريري والمخبري.

المرضى والطرق: تم اختيار ومراجعة الخزعات المأخوذة من المرضى المصابين بداء السكري من النوع ٢ لاشتباه معاناتهم بالمرض الكلوي غير الناجم عن داء السكري بين الفترة من يناير ٢٠٠٦م إلى ديسمبر ٢٠٠٨م في مستشفى واحد. تم تحليل البيانات السريرية والمخبرية ومقارنتها مع نتائج فحص الباثولوجي، وتقسيم المرضى إلى مجموعتين المجموعة الأولى تتألف من المصابين بتصلب الكبيبات السكري فقط والمجموعة الثانية من المصابين بالمرض الكلوي غير السكري بالإضافة إلى المصابين بتصلب الكبيبات السكري.

النتائج: تم أخذ ٣١ خزعة من المصابين بداء السكري من النوع الثاني، ١٧ مريضاً من الذكور (٥٤,٨٪) ويبلغ المتوسط العمري ٥٠,٦٨±١١,٢٩ عاماً. والفترة الرئيسية منذ الإصابة بالسكري ٩,٣٣±٣,٦ عاماً. أظهرت نتائج الخزعة أن ١٤ مريضاً (٤٥,٢٪) مصابين بالمرض الكلوي غير السكري مختلطاً بتصلب الكبيبات السكري، وكان التهاب الكبيبات الكلوي الهلالي أكثر النتائج شيوعاً حيث ظهر في ٣ حالات (٢١,٤٪ من المجموعة الثانية) تلاه الالتهاب الكلوي الخلالي الأنبوبي الحاد وتغيرات بسبب ارتفاع ضغط الدم الذي ظهر كل منهما لدى حالتين (١٤,٤٪). كما شملت النتائج اعتلالاً كلوياً بالغلوبولين المناعي A وتصلب الكبيبات المقطعي البؤري الأولي وانحلال عضلي والتهاب كبيبات الكلى الغشائي التكاثري حيث ظهر كل منها في حالة واحدة (٧,١٪). وكان مستوى البيلة البروتينية لدى المجموعة الأولى أعلى بكثير حيث قدر بـ ٤,٩٧ ± ٢,٠٨ غرام/٢٤ ساعة في البول بالمقارنة مع المجموعة الثانية الذي قدر بـ ٢,٧٢ ± ١,٠٩ غرام/٢٤ ساعة في البول (P = ٠,٠٠٣). لم نجد اختلافاً كبيراً بين المجموعتين من ناحية العمر أو فترة الإصابة بداء السكري أو الجنس أو الإصابة بارتفاع ضغط الدم أو البيلة الدموية أو كرياتينين المصل أو معدل ترشيح الكبيبات.

الاستنتاج: أظهرت نتائج الدراسة أن التهاب الكبيات الكلوي الهلالي هو المرض الكلوي السكري الأكثر شيوعاً بين مرضى السكري. وقد سجلت النتائج أن مستوى البيلة البروتينية مرتفع لدى المصابين بالمرض الكلوي السكري المتداخل مع تصلب الكبيبات الكلوي. لذا يجب أخذ الخزعة الكلوية من مرضى السكري عندما تكون الحالة السريرية غير نمطية.

مراشح الوريد الأجوف السفلي: خبرة ٥ سنوات في مركز رعاية متخصص

مقدمة: يُحبذ إعتراض مجرى الوريد الأجوف السفلي في حالات معينة لمنع حدوث انصمام رئوي، علماً بأن البيانات المتعلقة بالفعالية ومعدل الإختلاطات تتفاوت بشدة.

المرضى والطرق: أجرينا دراسة استعادية لمرضى عولجوا بتثبيت مرشحة مؤقتة أو دائمة في الوريد الأجوف السفلي في مستشفانا خلال السنوات الخمس الماضية.

النتائج: أُجريت عملية تثبيت مرشحة في الوريد الأجوف السفلي لسبع وسبعين مريضاً من أصل ٢٢٥ (٣٤٪) عانوا من خثار وريدي. شكل الخثار الوريدي العميق أكثر الأسباب توارداً للعلاج بمانعات التخثر. وكان حدوث النزف هو السبب في تثبيت مرشحة في الوريد الأجوف السفلي عند ٤٨ حالة (٦٢٪). عانى مريض واحد (١) من إختلاطات مرتبطة بهذا الإجراء. بينما عانى ٣ مرضى (من أصل ١٠) من معاودة الخثار الوريدي بعد إنقطاع طويل عن مانع التخثر.

الاستنتاج: تنسجم معاييرنا لاستطباب تثبيت مرشحة في الوريد الأجوف السفلي مع معايير الرعاية الراهنة. كانت الإختلاطات العاجلة والأجلة المرتبطة بتثبيت مرشحة في الوريد الأجوف السفلي متدنية. كان النزف النشط هو السبب الأكثر شيوعاً لتثبيت المرشحة، بينما كان إعتلال الخثار الوراثي شائعاً نسبياً.

أداء مؤشر كتلة الجسم في التنبؤ بداء السكري وارتفاع ضغط الدم في المنطقة الشرقية في المملكة العربية السعودية

مقدمة: يعتبر مؤشر كتلة الجسم المقياس الأكثر استخداماً لتحديد السمنة والتنبؤ بمضاعفاتها مثل السكري وارتفاع ضغط الدم. لكن دقته وفائدته لهذا الغرض غير معروفة لدى السعوديين. الهدف من هذه الدراسة هو تقييم صحة القيم التي يحددها مؤشر كتلة الجسم لدى الشعب السعودي في تحديد عوامل الخطر الأيضية.

المرضى والطرق: شارك ١٩٧، ٦٨١ شخص بالغ في دراسة مقطعية مستعرضة للكشف عن السكري وارتفاع ضغط الدم في المنطقة الشرقية بالمملكة في ٢٠٠٤م/٢٠٠٥م مع إجراء فحص ضغط الدم وسكر الدم أثناء الصوم وقياس الطول والوزن. وتم تحديد نسب الحساسية والمواصفات المعينة والمناطق تحت المنحنيات والقيمة التنبؤية والنسب المحتملة والنتائج الإيجابية الخاطئة والنتائج السلبية الخاطئة ومجموع نسب أخطاء التصنيف لمختلف نسب مؤشرات كتلة الجسم باستخدام منحنيات ROC، وتقييم أهمية الربط بين عوامل الخطر الأيضية ومؤشر كتلة الجسم باستخدام تحليل الانحدار.

النتائج: فيما يتعلق بالسمنة المفرطة فقد أظهر تحليل منحنى ROC أن الحد الأمثل لمؤشر كتلة الجسم يتراوح بين ٢٨,٥ و٢٩,٥ لدى الرجال وبين ٣٠,٥ و٣١,٥ لدى النساء، إلا أن مستويات الحساسية والمواصفات المعينة كانت قليلة جداً لدرجة تجاهلها من الناحية السريرية، وكان المجموع العام لسوء التصنيف مرتفع لدرجة غير مقبولة عند جميع نسب مؤشرات كتلة الجسم (٠,٨٠). ولم تتحسن العلاقة بين مؤشر كتلة الجسم والإصابة بالسكري و/أو ارتفاع ضغط الدم عند ٢٥ من مؤشرات كتلة الجسم. وباستخدام تحليل الانحدار فقد ارتفعت نسبة الاحتمالات بارتفاع ضغط الدم و/أو السكري بشكل تدريجي واضح عند مؤشر كتلة الجسم المنخفضة ٢١-٢٣ دون تحسن في التشخيص الأدائي لمؤشر كتلة الجسم عند هذا الحد.

الاستنتاج: وجدنا ارتفاعاً في نسب الإصابة بالسكري وارتفاع ضغط الدم لدى شريحة كبيرة من سكان المنطقة الشرقية بالمملكة العربية السعودية المتعلقة بمؤشر كتلة الجسم حتى قيمة منخفض وصلت إلى ٢١ من مؤشر كتلة الجسم. لكن بشكل عام لا يوجد مستوى معين لمؤشر كتلة الجسم يمكن تحديده لتنبؤ الإصابة بهذه الأمراض المزمنة بما فيها تعريف منظمة الصحة العالمية للسمنة عند ٣٠ من قيمة مؤشر كتلة الجسم.

التهاب الشغاف الجرثومي في مستشفى في المملكة العربية السعودية: الوبائية، والبكتيريا الممرضة والمآل

مقدمة: لا يتوفر سوى القليل من المعلومات حول انتشار التهاب الشغاف الجرثومي ووبائياته ومسبباته في المملكة العربية السعودية ومنطقة الخليج. وفي هذه الدراسة قمنا بوصف نمط التهاب الشغاف والعوامل المسببة له في أحد مستشفيات المملكة العربية السعودية.

المرضى والطرق: أجرينا تحليلاً استعادياً لجميع حالات التهاب الشغاف المبلغ عنها في مركز الظهران الصحي من يناير ١٩٩٥م وحتى ديسمبر ٢٠٠٨م.

النتائج: من بين ٨٣ حالة التهاب الشغاف وجدنا ٥٤ حالة مؤكدة (٦٥٪). أما الحالات المتبقية البالغ عددها ٢٩ (٣٥٪) فهي حالات محتملة لالتهاب الشغاف بناءً على معايير ديوك Duke Criteria. شملت حالات التهاب الشغاف المؤكدة ٣٩ ذكراً و١٥ أنثى (بنسبة ٢,٦:١)، وكان متوسط العمر (الانحراف المعياري) ٥٩,٧ عاماً (١٨,٢). ومن بين حالات التهاب الشغاف المؤكدة حدث التهاب الشغاف في صمام طبيعي في ٤٤ حالة (٨١,٥٪) ولوحظ في صمام صناعي في ١٠ حالات (١٨,٥٪). كان أكثر الصمامات المصابة بهذا الالتهاب هو الصمام التاجي (العدد=٢٤؛ ٤٤,٤٪)، والصمام الأبهري (العدد=٢٠؛ ٣٩,٢٪). أما أكثر أنواع البكتيريا شيوعاً فهي: العنقودية الذهبية *Staphylococcus aureus* (العدد=٢٣؛ ٤٢,٦٪)، والمكورة المعوية البرازية *Enterococcus* Faecalis (العدد=١٢؛ ٢٢,٢٪)، والعقديات المخضرة *Viridans streptococci* (العدد=٩؛ ١٦,٧٪). كان التدخل الجراحي ضرورياً في ١٧ حالة (٣١,٤٪) وبلغ معدل الوفيات أثناء التنوم في المستشفى ٢٩,٤٪ (العدد=١٥). وتعرض ٣ (٥,٥٪) من المرضى لسكتة دماغية انصمامية كإحدى المضاعفات.

الاستنتاج: النوع السائد من التهاب الشغاف هو ذلك الذي يصيب الصمامات الطبيعية. أما المرضى فهم من البالغين الأكبر سناً، وأكثر أنواع البكتيريا شيوعاً هي العنقودية الذهبية والمكورة المعوية البرازية والعقديات المخضرة.

تجربة سريرية استباقية عشوائية تقارن عملية الاستئصال البلازمي الحركي ذو القطبين للبروستات مقابل عملية الاستئصال أحادي القطب عبر الاحليل للبروستات في علاج فرط التنسج الحميد في البروستات

مقدمة: إن عملية استئصال البروستات باستخدام العروة البلازمية الحركية هي البديل لعملية الاستئصال أحادي القطب عبر الاحليل للبروستات من أجل علاج فرط التنسج الحميد في البروستات. قمنا بمقارنة نتائج العلاجين في تجربة عشوائية.

المرضى والطرق: قمنا على مدى سنة باختيار مرضى بشكل عشوائي لديهم استطباب للعلاج بالعملية من أجل فرط التنسج الحميد في البروستات وتنطبق عليهم معايير العلاج إما بالاستئصال باستخدام العروة البلازمية الحركية أو بالاستئصال أحادي القطب عبر الاحليل للبروستات. قمنا بتسجيل ما يلي: قياس حجم البروستات باستخدام التصوير بالموجات فوق الصوتية عبر المستقيم، زوال الانسداد في مخرج المثانة، مدة العملية، تدهور مصل الصوديوم والهيموغلوبين، وزن رقاقات البروستات المستأصلة، مدة القسطرة والتنويم في المستشفى. تم تقييم المرضى بعد شهر واحد من خروجهم من المستشفى من أجل أعراض الانسداد. كما تم تسجيل المضاعفات.

النتائج: خضع ٥١ مريضاً من بين ١٠٢ مريضاً لعملية استئصال باستخدام العروة البلازمية الحركية للبروستات (PKRP) و٥١ لعملية استئصال أحادي القطب عبر الاحليل للبروستات (TURP). لم تظهر إزالة أعراض الانسداد ومتوسط مدة العملية اختلافاً إحصائياً كبيراً. كان تدهور الهيموغلوبين في المجموعة التي خضعت لعملية استئصال البروستات باستخدام العروة البلازمية الحركية عروة البلازما الحركية للبروستات (PKRP) أقل من المجموعة التي خضعت لعملية استئصال البروستات أحادي القطب عبر الاحليل (TURP) (٠,٦ g/dL vs ١,٨ g/dL, P=.٠١)، وانخفاض أقل في مستويات الصوديوم في المصل (١,٠٣ mmol/L vs ٥,٠١ mmol/L, P=.٠١)، ومدة قسطرة أقل (٣٧,٢ ساعة مقابل ٥٧,٧ ساعة، P=.٠٣) بالإضافة إلى مدة تنويم أقل (١,٥ يوم مقابل ٢,٦ يوم، P=.٠٢). احتاج مريض واحد، في المجموعة التي خضعت لعملية استئصال البروستات باستخدام العروة البلازمية الحركية (PKRP)، إلى إعادة قسطرة مقابل أربعة مرضى في المجموعة التي خضعت لعملية استئصال البروستات أحادي القطب عبر الاحليل (TURP)

الاستنتاج: تقلل عملية استئصال البروستات باستخدام العروة البلازمية الحركية (PKRP) من نسبة انتشار المرض مع نتائج مشابهة لعملية الاستئصال أحادي القطب عبر الاحليل التقليدية لعلاج فرط التنسج الحميد في البروستات.

الخلاصات العربية

المدونات الطبية السعودية

تصدر المدونات الطبية السعودية مرة كل شهرين عن مستشفى الملك فيصل التخصصي ومركز الأبحاث ، ص.ب ٣٣٥٤ ، الرياض ١١٢١١. المملكة العربية السعودية. يتم توزيع المدونات وإعداد الملخصات العربية بالتعاون مع د. زهير القاوي بواسطة موظفي إدارة الخدمات الإدارية بمستشفى الملك فيصل التخصّصي ومركز الأبحاث. جميع المراسلات والاستفسارات وطلبات الاشتراك ترسل إلى المحرر الأول مكتب المطبوعات (ر.إ ٣٦).

سعر الاشتراك ١٠٠ ريال في السنة للأفراد داخل المملكة و٢٠٠ ريال في السنة للأفراد خارج المملكة و٥٠٠ ريال في السنة للمؤسسات. يمكن فتح اشتراك مجاني للأفراد و المؤسسات في الدول النامية.

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مكتب التحرير:
المدونات الطبية السعودية (ر.إ ٣٦)
مستشفى الملك فيصل التخصّصي ومركز الأبحاث ،
ص.ب ٣٣٥٤
الرياض ١١٢١١
المملكة العربية السعودية
هاتف: ٤٦٤٧٢٧٢-١-٩٦٦ تحويلة ٣١٨١٩/٣١٨١٥
فاكس: ٤٦٤٧٢٧٢-١-٩٦٦ تحويلة ٣١٨٧٥
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مجلة المدونات الطبية السعودية مفهرسة بواسطة الفهرس الطبي (المكتبة الوطنية للطب)، والفهرس الطبي لمنظمة الصحة العالمية • إقليم شرق المتوسط، المحتويات الراهنة، التجارب الطبية، الوعي الراهن في العلوم الحيوية، الفهرس التراكمي للتمريض والعلوم الصحية المساعدة، الجمعية الأمريكية اللاتينية للمعلومات العلمية.

الرقم التسلسلي القياسي الدولي: ٠٢٥٦ - ٤٩٤٧
١٤٢٧-٠٤

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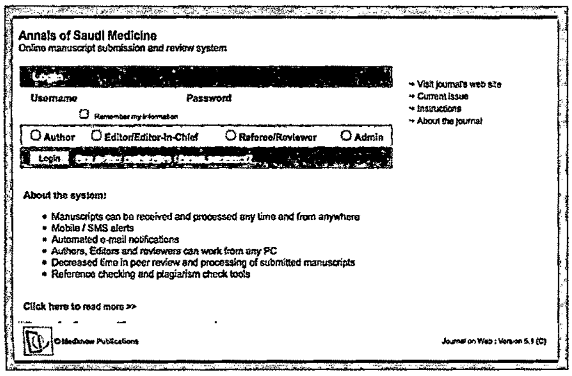
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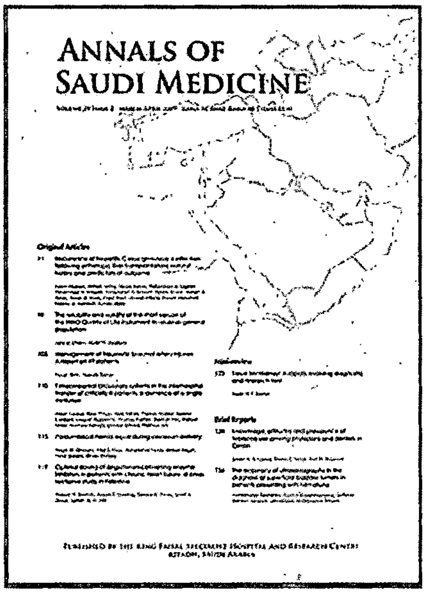

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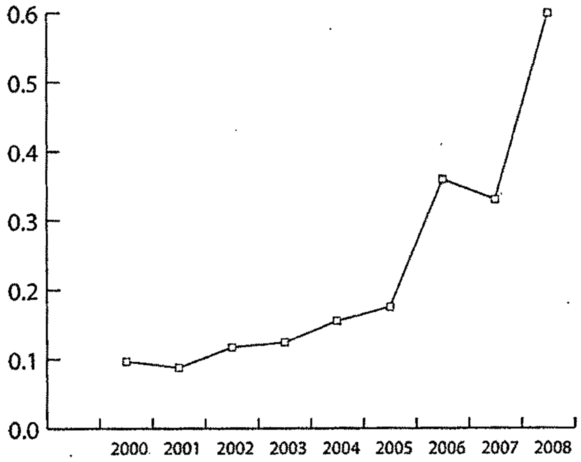

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